January 14, 2003

TO: Catherine Serke, Art Unit 3763
CP2, Room 3-E-16

FROM: Jeanne Horrigan, EIC-3700

SUBJECT: Search Results for Serial #09/344735

Attached are the search results for the "Synergism of Photodynamic and Electropermeation Effects on Cell Vitality ...," including results of prior art and inventor searches in foreign patent databases, and prior art searches in medical, biotech, and general sci/tech non-patent databases.

I tagged the items that seemed to me to be most relevant, but **I suggest that you review all of the results**.

Also attached is a "*Search Results Feedback Form*." Your feedback will help enhance our search services.

I hope these results are useful. Please let me know if you would like me to expand or modify the search or if you have any questions.

Access DB# 84098

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Catherine Seidel Examiner #: 7029 Date: 1/13/02
Art Unit: 3763 Phone Number 308-4846 Serial Number: 09/344,735
Mail Box and Bldg/Room Location: 3E116 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Synergism of photodynamic and electropermeation effects on cell vitality as a novel cytotoxic agent

Inventors (please provide full names): ~~Xing Hang~~, Herman Berg, Maya Lambrova

Earliest Priority Filing Date: 01/26/98

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

A method for inhibiting cell growth
- applying a photosensitive agent to a cell
- applying an electric pulse to electroporate the cell
- applying light to photoactivate the photosensitive agent to inhibit cell growth or enhance cell death

****

STAFF USE ONLY

Searcher: JEANNE HORRIGAN
Searcher Phone #: 305-0934
Searcher Location: CP2-2008
Date Searcher Picked Up: 1/13
Date Completed: 1/14
Searcher Prep & Review Time: 171
Clerical Prep Time: _____
Online Time: 129

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic ✓
Litigation _____
Fulltext ✓
Patent Family _____
Other _____

Vendors and cost where applicable

STN _____
Dialog ✓
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

2.45 -

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File 350:Derwent WPIX 1963-2002/UD,UM &UP=200303
         (c) 2003  Thomson Derwent
File 344:Chinese Patents Abs Aug 1985-2002/Nov
         (c) 2002 European Patent Office
File 347:JAPIO Oct 1976-2002/Sep(Updated 030102)
         (c) 2003 JPO & JAPIO
File 371:French Patents 1961-2002/BOPI 200209
         (c) 2002 INPI.  All rts. reserv.

Set     Items   Description
S1     505997   CELL? ?
S2       8831   SURVIV?
S3     205212   DEATH OR DIE OR DIES OR DIED OR DYING
S4     150205   GROWTH
S5     264109   INHIBIT???
S6     707286   STOP? ? OR STOPP???
S7       4243   AVERT???
S8     227094   CHECK???
S9       1946   CURB???
S10      3315   APOPTOSIS
S11       984   S1(2N)S2
S12      2171   S1(3N)S3
S13      3207   S1(2N)S4(3N)S5:S9
S14      6029   S11:S13
S15      1441   ELECTROPORAT?
S16     10087   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17         7   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18       730   IONTOPHORESIS
S19     12144   S15:S18
S20    244193   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21      1508   PHOTODYNAMIC()THERAPY OR PDT
S22        72   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    245560   S20:S22
S24         1   S14 AND S19 AND S23
S25   4018080   ELECTR?
S26         3   S14 AND S23 AND S25
S27         2   S26 NOT S24
```

24/26,TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

duplicate of tagged patent in inventors' search results.

012988790
WPI Acc No: 2000-160643/200014

Inhibiting cell growth or enhancing cell death by electroporation of a photosensitive agent in a cell and photo-activation of the agent, useful for treating cancers and tumors

27/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014688434 **Image available**
WPI Acc No: 2002-509138/200254

Medical laser instrument for photodynamic treatment using a semiconductor laser diode has laser diode complex acting as laser beam source which is shaped by condensing lens

Patent Assignee: BAHK J (BAHK-I)
Inventor: BAHK J

Number of Countries: 086 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200254968	A1	20020718	WO 2002KR7	A	20020104	200254	B

Priority Applications (No Type Date): KR 20011224 A 20010109
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200254968	A1	E	13	A61B-018/20	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): EA GH GM KE LS MW MZ OA SD SL SZ TZ UG ZM ZW

Abstract (Basic): WO 200254968 A1

NOVELTY - Instrument uses only the laser beam as excitation medium for photodynamic reaction, which causes release of fluorescent light or free radical oxygen within the cells that contain non-toxic **photosensitizers** . Abnormal cells retain **photosensitizers** , which when irradiated by laser of specific wavelength release free radical oxygen that is toxic to the **cell** , causing **death** of the **cell** . Normal cells which do not retain the **photosensitizers** do not develop photo-reaction

DETAILED DESCRIPTION - Instrument casing (1) has small holes in its side for ventilation air to pass in and out of casing, which also accommodates a filter located next to a fan. Power is connected to power input cord (2) placed at the case. AC power is applied through a DC converter (3) located inside the case. DC **electric** circuit is connected to a main control panel (4) inside the case. The **electric** circuit passes through a first switch (5), then it is connected to a switch converter (8), then it is connected to either the second switch (6) or a pedal switch (7), then the **electric** circuit is connected to the high power semiconductor laser diode, and the **electric** circuit is again connected to the control panel.

USE - For photodynamic treatment or photodynamic diagnosis without use of heating aspect of laser energy.

ADVANTAGE - A laser beam that has different wavelengths will prevent **photosensitization** and overlapping with absorption band of hemoglobin. The use of a semiconductor laser diode reduces the size, price and maintenance cost.

DESCRIPTION OF DRAWING(S) - The drawing shows a layout of the instrument.

Case (1)
AC input (2)
DC converter (3)
Controller (4)
First and second switches (5,6)
Pedal switch (7)
Switch converter (8)
Semiconductor laser diode (9)
pp; 13 DwgNo 1/2

Derwent Class: P31; S03; S05; U12; V08
International Patent Class (Main): A61B-018/20

?t27/3,k/2

27/3,K/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014334156 **Image available**
WPI Acc No: 2002-154859/200220
XRAM Acc No: C02-048446
XRPX Acc No: N02-117732

Non-thermal device for treating and/or curing cardiac arrhythmias, and electrically isolating pulmonary vein from right atrium and for delivering fluoroscopic contrast agent for coronary angiography

Patent Assignee: UNIV JOHNS HOPKINS (UYJO); LARDO A C (LARD-I); SUSIL R C (SUSI-I)
Inventor: LARDO A C; SUSIL R C
Number of Countries: 095 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200203872	A2	20020117	WO 2001US41343	A	20010711	200220 B
AU 200218742	A	20020121	AU 200218742	A	20010711	200234
US 20020095197	A1	20020718	US 2000217522	A	20000711	200254
			US 2001904182	A	20010711	

Priority Applications (No Type Date): US 2000217522 P 20000711; US 2001904182 A 20010711
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200203872	A2	E	25	A61B-018/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200218742	A	A61B-018/00	Based on patent WO 200203872
US 20020095197	A1	A61M-025/10	Provisional application US 2000217522

Non-thermal device for treating and/or curing cardiac arrhythmias, and electrically isolating pulmonary vein from right atrium and for delivering fluoroscopic contrast agent for coronary angiography

Abstract (Basic):
... or curing cardiac arrhythmias using photo-chemotherapy or photo-dynamic therapy; (vi) A method to **electrically** isolate the pulmonary vein from the left atrium using photo-chemotherapy or photo-dynamic therapy...

...using photo-chemotherapy or photo-dynamic therapy; and (viii) A photo-dynamic method for causing **cell death** in certain cardiac tissue such that **electrical** rhythms cannot be generated and/or sustained...

...For treating and/or curing cardiac arrhythmias, for ablation of pulmonary vein ostia and **electrically** isolating pulmonary vein from right atrium (all claimed), for treating paroxysmal atrial fibrillation, and for...

...pathways from which abnormal signals arising and/or destroy other cardiac tissue, such that abnormal **electrical** rhythm can be sustained. The photo-chemotherapy does not destroy tissues through either heating or...

...function. The photo-chemotherapy enables greater success in creating continuous and uniform lesions. Since the **photosensitizing** agent need only to be delivered to myocardium, the agent is perfused directly into the...

Technology Focus:

... near its distal end and a light source located within the balloon or reservoir. A **photosensitizing** agent such as porfimer sodium or phthalocyanines, is perfused into and delivered by the balloon to a desired treatment site and light capable of activating the **photosensitizing** agent is delivered by the light source through the balloon and to the desired treatment...

...into the treatment area. The fiber provides illumination at a wavelength capable of activating the **photosensitizing** agent. A dual function catheter is combined with a high-resolution imaging and photo-chemotherapy...

...pathways from which abnormal signals arise and/or in other cardiac tissues such that abnormal **electrical** rhythms cannot be generated and/or sustained. photo-dynamic method for causing **cell death** in certain cardiac tissue such that abnormal **electrical** rhythms cannot be generated and/or sustained. The device induces apoptopic **cell death** of tissues and pathways from which abnormal signals arise and/or in other cardiac tissues such that abnormal **electrical** rhythms cannot be generated and/or sustained. The **photosensitizing** agent is delivered to the cardiac tissue systematically, which is preferentially absorbed by the tissues and pathways from which abnormal signals causing the arrhythmias arise, and the **photosensitizing** agent is activated with an illumination mechanism. The activation by illumination mechanism overlaps with the...

...Title Terms: **ELECTRIC ;**

File 348:EUROPEAN PATENTS 1978-2003/Jan W01
(c) 2003 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030109,UT=20030102
(c) 2003 WIPO/Univentio

Set	Items	Description
S1	406296	CELL? ?
S2	41778	SURVIV?
S3	137095	GROWTH
S4	213092	INHIBIT???
S5	280972	STOP? ? OR STOPP???
S6	4654	AVERT???
S7	154767	CHECK???
S8	2198	CURB???
S9	10466	APOPTOSIS
S10	9399	S1(2N)S2
S11	34639	S1(3N)S3
S12	1916	S1(2N)S4(3N)S5:S9
S13	20981	ELECTROPORAT?
S14	8353	(DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S15	1936	ELECTRIC??()PATCH?? OR IONTOPHORESIS OR IONTOTHERAPY OR IONOTHERAPY OR ION()MEDICATION? ?
S16	29433	S13:S15
S17	27108	PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S18	1606	PHOTODYNAMIC()THERAPY OR PDT
S19	202	PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S20	28243	S17:S19
S21	1	S16/TI,AB AND S10:S12 AND S20
S22	295	S16 AND S20 AND S10:S12
S23	294	S22 NOT S21
S24	207	S1/TI,AB AND S23
S25	7	S10:S12/TI,AB AND S16 AND S20
S26	6	S25 NOT S21
S27	1	S16/TI,AB AND S10:S12 AND S20
S28	0	S27 NOT S25
S29	8	(S20/TI,AB AND S16 AND S10:S12) NOT S25

21/3,AB/1 (Item 1 from file: 349) a duplicate
DIALOG(R)File 349:PCT FULLTEXT

00536877

SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT

SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE

Patent Applicant/Assignee:
GENETRONICS INC,
Inventor(s):
LAMBREVA Maya,
BERG Hermann,

Patent and Priority Information (Country, Number, Date):
Patent: WO 200000250 A1 20000106 (WO 0000250)
Application: WO 99US14202 19990625 (PCT/WO US9914202)
Priority Application: US 9890751 19980626
Designated States: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 9253

English Abstract

The present invention is based on the discovery that **electroporation** of a **photosensitive** agent in a cell and subsequent activation of the agent provides more effective killing of the **electroporated** cell than cells exposed to a **photosensitive** agent alone. The invention provides a method and apparatus for inhibiting **cell growth** or enhancing **cell** death. The method includes providing a **photosensitive** agent to a cell; applying an **electric pulse** to the cell of a sufficient strength and duration to **electroporate** the cell with the **photosensitive** agent; and applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting **cell growth** or enhancing **cell** death.

26/6/1 (Item 1 from file: 349)
00885422 **Image available**
SCANNING FLUORESCENCE LIFETIME MICROSCOPE: DIRECTED EVOLUTION
MICROSCOPE DE DETERMINATION DE LA DUREE DE VIE DE FLUORESCENCE A BALAYAGE A INTERFACE INFORMATIQUE UTILISE DANS LES TECHNIQUES D'EVOLUTION DIRIGEE ET METHODES DE STRUCTURATION PHOTO-INDUITE UTILISEES DANS LA SELECTION CELLULAIRE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 13524
Publication Year: 2002

26/6/2 (Item 2 from file: 349)
00807978
METHODS FOR TARGETING CELLS **THAT EXPRESS FIBROBLAST** GROWTH **RECEPTOR-3 OR-2**
PROCEDES CIBLANT LES CELLULES EXPRIMANT LES RECEPTEURS 2 ET 3 DE CROISSANCE DES FIBROBLASTES
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 21656
Publication Year: 2001

26/6/3 (Item 3 from file: 349)
00754459
ESTROGEN SIGNALLING PATHWAY REGULATORS AND USES THEREOF
REGULATEURS DU CANAL DE SIGNALISATION DES OESTROGENES ET UTILISATIONS CORRESPONDANTES
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 22021
Publication Year: 2000

26/6/4 (Item 4 from file: 349)
00741288
APOPTOSIS INDUCING MOLECULE II AND METHODS OF USE
MOLECULE II INDUISANT L'APOPTOSE ET TECHNIQUES D'UTILISATION
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 113950
Publication Year: 2000

26/6/5 (Item 5 from file: 349)
00427221
DNA SEQUENCES ENCODING FUSIONS OF DNA REPAIR PROTEINS AND USES THEREOF
SEQUENCES D'ADN CODANT DES PROTEINES HYBRIDES DE REPARATION DE L'ADN ET UTILISATIONS DESDITES SEQUENCES
Publication Language: English
Fulltext Availability:
Detailed Description

Claims
Fulltext Word Count: 42745
Publication Year: 1998

26/6/6 (Item 6 from file: 349)
00241471 **Image available**
NOVEL GENE THERAPIES EMPLOYING ANTISENSE CONSTRUCTS
NOUVELLES THERAPIES GENIQUES METTANT EN OEUVRE DES STRUCTURES NON CODANTES
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 9700
Publication Year: 1993

29/6/1 (Item 1 from file: 348)
00765472
TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS BY PHOTOSENSITIZING **COMPOUNDS**
TRANSFER VON MOLEKULEN IN DAS ZYTOSOL VON ZELLEN DURCH PHOTOSENSIBILISIERENDE SUBSTANZEN
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE AU MOYEN DE COMPOSES PHOTOSENSIBILISANTS
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200148	1115
CLAIMS B	(German)	200148	1038
CLAIMS B	(French)	200148	1146
SPEC B	(English)	200148	3687
Total word count - document A			0
Total word count - document B			6986
Total word count - documents A + B			6986

29/6/2 (Item 1 from file: 349)
00911642
PHOTOCHEMICAL INTERNALIZATION FOR VIRUS-MEDIATED MOLECULE DELIVERY INTO THE CYOSOL
INTERNALISATION PHOTOCHIMIQUE POUR INTRODUCTION DE MOLECULES DANS LE CYTOSOL PAR DES VECTEURS VIRAUX
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 17729
Publication Year: 2002

29/6/3 (Item 2 from file: 349)
00868394 **Image available**
USE OF INDOLE-3-ACETIC ACID DERIVATIVES IN MEDICINE
UTILISATION DE DERIVES D'ACIDE INDOLE-3-ACETIQUE EN MEDECINE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 13771
Publication Year: 2002

29/6/4 (Item 3 from file: 349)
00739696
PHOTODYNAMIC THERAPY **IN COMBINATION WITH APOPTOSIS INDUCING FACTORS**
THERAPIE PHOTODYNAMIQUE ASSOCIEE A DES FACTEURS INDUISANT L'APOPTOSE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 14620
Publication Year: 2000

29/6/5 (Item 4 from file: 349)
00460905 **Image available**
GLOBAL MEDICAL TREATMENT METHOD AND APPARATUS
DISPOSITIF ET TROUSSE POUR TRAITEMENT MEDICAL GLOBAL
Publication Language: English
Fulltext Availability:

Detailed Description
Claims
Fulltext Word Count: 15630
Publication Year: 1998

29/6/6 (Item 5 from file: 349)
00431567 **Image available**
SKIN VIBRATION METHOD FOR TOPICAL TARGETED DELIVERY OF BENEFICIAL AGENTS INTO HAIR FOLLICLES
METHODE POUR FAIRE VIBRER LA PEAU, PERMETTANT DE LIBERER LOCALEMENT ET DE MANIERE CIBLEE DES AGENTS BENEFIQUES DANS LES FOLLICULES PILEUX
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5698
Publication Year: 1998

29/6/7 (Item 6 from file: 349)
00393729
METHODS FOR INDUCING IMMUNE RESPONSIVENESS IN A SUBJECT
PROCEDE DESTINE A INDUIRE CHEZ UN SUJET UNE APTITUDE A LA REPONSE IMMUNITAIRE
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 17579
Publication Year: 1997

29/6/8 (Item 7 from file: 349)
00324924
TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 4835
Publication Year: 1996
?t29/3,ab/1,2,4,5,8

29/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00765472
TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS BY PHOTOSENSITIZING **COMPOUNDS**
TRANSFER VON MOLEKULEN IN DAS ZYTOSOL VON ZELLEN DURCH PHOTOSENSIBILISIERENDE SUBSTANZEN
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE AU MOYEN DE COMPOSES PHOTOSENSIBILISANTS
PATENT ASSIGNEE:
Photocure ASA, (2296583), Hoffsveien 48, 0377 Oslo, (NO), (Proprietor designated states: all)
INVENTOR:
BERG, Kristian, Vollenveien 158, 1380 Heggedal, (NO)
SANDVIK, Kirsten, Bestumveien 82A, 0283 Oslo, (NO)
MOAN, Johan, Osstubben 6, 0381 Oslo, (NO)
LEGAL REPRESENTATIVE:
Dzieglewska, Hanna Eva et al (73231), Frank B. Dehn & Co., European Patent Attorneys, 179 Queen Victoria Street, London EC4V 4EL, (GB)
PATENT (CC, No, Kind, Date): EP 783323 A1 970716 (Basic)

EP 783323 B1 011128
WO 9607432 960314
APPLICATION (CC, No, Date): EP 95932244 950904; WO 95NO149 950904
PRIORITY (CC, No, Date): NO 943327 940908
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; SI
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-047/00
NOTE:
No A-document published by EPO
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200148	1115
CLAIMS B	(German)	200148	1038
CLAIMS B	(French)	200148	1146
SPEC B	(English)	200148	3687
Total word count - document A			0
Total word count - document B			6986
Total word count - documents A + B			6986

29/3,AB/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00911642
PHOTOCHEMICAL INTERNALIZATION FOR VIRUS-MEDIATED MOLECULE DELIVERY INTO THE CYOSOL
INTERNALISATION PHOTOCHIMIQUE POUR INTRODUCTION DE MOLECULES DANS LE CYTOSOL PAR DES VECTEURS VIRAUX
Patent Applicant/Assignee:
THE NORWEGIAN RADIUM HOSPITAL RESEARCH FOUNDATION, Montebello, P.O. Box 56, N-0310 Oslo, NO, NO (Residence), NO (Nationality), (For all designated states except: US)
JONES Elizabeth Louise, Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL, GB, GB (Residence), GB (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
HOGSET Anders, Treskeveien 32A, N-0681 Oslo, NO, NO (Residence), NO (Nationality), (Designated only for: US)
BERG Kristian, Vollenvn. 158, N-1389 Heggedal, NO, NO (Residence), NO (Nationality), (Designated only for: US)
MAELANDSMO Gunnhild Mari, Olav Hegnas vei 7, N-0585 Oslo, NO, NO (Residence), NO (Nationality), (Designated only for: US)
ENGESAETER Birgit Ovstebo, Sollerudveien 14, N-0283 Oslo, NO, NO (Residence), NO (Nationality), (Designated only for: US)
PRASMICKAITE Lina, BREKKELIA 3E, N-0882 Oslo, NO, NO (Residence), LT (Nationality), (Designated only for: US)
Legal Representative:
JONES Elizabeth Louise (commercial rep.), Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL, GB,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200244395 A1 20020606 (WO 0244395)
Application: WO 2001GB5281 20011129 (PCT/WO GB0105281)
Priority Application: GB 200029142 20001129; GB 200029405 20001201; GB 200114696 20010615
Designated States: AE AG AL AM AT AT (utility model) AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ CZ (utility model) DE DE (utility model) DK DK (utility model) DM DZ EC EE EE (utility model) ES FI FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 17729

English Abstract
The present invention provides a method for introducing a molecule into the cytosol of a cell in which the cell is contacted with a **photosensitising** agent, the cell is irradiated with light of a wavelength effective to activate the **photosensitising** agent and, substantially at the same time or after the irradiation, the cell is contacted with the molecule to be introduced, particularly for use in cancer treatment, gene therapy and vaccination.

French Abstract
L'invention concerne un procede permettant d'introduire une molecule dans le cytosol d'une cellule. Ce procede consiste a faire entrer la cellule en contact avec un agent photosensibilisant, puis a irradier la cellule avec une lumiere presentant un longueur d'onde permettant d'activer l'agent photosensibilisant, et simultanement a cette irradiation ou apres cette derniere, a faire entrer la cellule en contact avec la molecule devant etre introduite. Ce procede convient en particulier pour les traitements anticancereux, les therapies geniques et les vaccinations.

29/3,AB/4 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00739696
PHOTODYNAMIC THERAPY **IN COMBINATION WITH APOPTOSIS INDUCING FACTORS**
THERAPIE PHOTODYNAMIQUE ASSOCIEE A DES FACTEURS INDUISANT L'APOPTOSE
Patent Applicant/Assignee:
QLT PHOTOTHERAPEUTICS INC, 887 Great Norther Way, Vancouver, British Columbia V5T 4T5, CA, CA (Residence), CA (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
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GRANVILLE David J, #34 - 1751 Paddock Drive, Coquitlam, British Columbia V5T 4T5, CA, CA (Residence), CA (Nationality), (Designated only for: US)
Legal Representative:
ROBINSON J Christopher, Fetherstonhaugh & Co., Suite 2200, 650 West Georgia Street, Box 11560, Vancouver, British Columbia V6B 4N8, CA
Patent and Priority Information (Country, Number, Date):
Patent: WO 200051638 A1 20000908 (WO 0051638)
Application: WO 2000CA200 20000225 (PCT/WO CA0000200)
Priority Application: US 99121770 19990226
Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 14620

English Abstract
The invention relates to **photodynamic therapy** (**PDT**) used in combination with apoptosis-inducing agents to destroy target cells and

tissues. Benefits of such combinations include 1) the ability to use lower doses of **photosensitizers** and/or light; 2) the ability to use lower doses of apoptosis-inducing agents; and 3) the ability to use apoptosis-inducing agents against target tissues which are otherwise insensitive to the apoptosis-inducing agents.

French Abstract
La presente invention concerne la therapie photodynamique (TPD) utilisee en association a des agents induisant l'apoptose, dans le but de detruire les tissus et les cellules cibles. Les avantages de ces associations consistent en: 1) la possibilite d'utiliser des doses inferieures de photosensibilisants et/ou de lumiere; 2) la possibilite d'utiliser des doses inferieures d'agents induisant l'apoptose; et 3) la possibilite d'utiliser des agents induisant l'apoptose contre des tissus cibles qui sont sinon insensibles aux agents induisant l'apoptose.

29/3,AB/5 (Item 4 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00460905
GLOBAL MEDICAL TREATMENT METHOD AND APPARATUS
DISPOSITIF ET TROUSSE POUR TRAITEMENT MEDICAL GLOBAL
Patent Applicant/Assignee:
EDWARDS Stuart D,
Inventor(s):
EDWARDS Stuart D,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9851369 A1 19981119
Application: WO 98US9840 19980513 (PCT/WO US9809840)
Priority Application: US 9746356 19970513; US 9746729 19970516
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 15630

English Abstract
A kit includes a medicament delivery device including a medicament housing with a drug delivery reservoir and a membrane coupled to the medicament housing. The kit further includes a medicament selected from the group of a chemotherapeutic agent, immunotherapeutic agent, cell, anti-angiogenic agent, vascular sealing agent, gene therapy agent, antibiotic, resistance modification agent and a **photodynamic therapy** agent.

French Abstract
L'invention concerne une trousse comportant un dispositif d'administration de medicament, qui comprend un logement de medicament muni d'un reservoir d'administration de medicament et une membrane couplee au logement de medicament. La trousse comporte en outre un medicament selectionne dans le groupe constitue par un agent chimiotherapeutique, un agent immunotherapeutique, une cellule, un agent anti-angiogenique, un agent d'obturation vasculaire, un agent de therapie genique, un antibiotique, un agent de modification de resistance et un agent de therapie photodynamique.

29/3,AB/8 (Item 7 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00324924

TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE

Patent Applicant/Assignee:
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BERG Kristian,
SANDVIK Kirsten,
MOAN Johan,
Inventor(s):
BERG Kristian,
SANDVIK Kirsten,
MOAN Johan,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9607432 A1 19960314
Application: WO 95NO149 19950904 (PCT/WO NO9500149)
Priority Application: NO 943327 19940908
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 4835

English Abstract
A method for releasing molecules into the cytosol of cells without killing the majority of the cells by allowing the molecules to be taken up in endosomes, lysosomes or other cell compartments and use light activation of **photosensitizing** compounds to rupture the membranes of the endosomes, lysosomes or other cell compartments, is described.

File 348:EUROPEAN PATENTS 1978-2003/Jan W01
(c) 2003 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030109,UT=20030102
(c) 2003 WIPO/Univentio

Set	Items	Description
S1	406296	CELL? ?
S2	41778	SURVIV?
S3	137095	GROWTH
S4	213092	INHIBIT???
S5	280972	STOP? ? OR STOPP???
S6	4654	AVERT???
S7	154767	CHECK???
S8	2198	CURB???
S9	10466	APOPTOSIS
S10	9399	S1(2N)S2
S11	34639	S1(3N)S3
S12	1916	S1(2N)S4(3N)S5:S9
S13	20981	ELECTROPORAT?
S14	8353	(DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S15	39	ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IONOTHERAPY OR ION()MEDICATION? ?
S16	1915	IONTOPHORESIS
S17	27108	PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S18	1606	PHOTODYNAMIC()THERAPY OR PDT
S19	202	PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S20	0	S20:S22
S21	0	S14 AND S19 AND S23
S22	28042	S13:S15
S23	30058	S16:S19
S24	71	S12 AND S22 AND S23
S25	1	S12(S)S22(S)S23
S26	378	IC=A61N-001/00
S27	1	S24 AND S26
S28	1	S27 NOT S25
S29	38058	S10:S12
S30	3	S29 (S)S22(S)S23
S31	3	S30 NOT S27:S28
S32	83	(S29 AND S22(S)S23) NOT (S30 OR S25 OR S27)
S33	3	S29 AND S22 AND S23 AND S26
S34	2	S33 NOT S30
S35	1	S22/TI,AB AND S29(S)S23
S36	7	S22/TI,AB AND S29 AND S23
S37	6	S36 NOT (S35 OR S30 OR S25 OR S27)

25/6/1 (Item 1 from file: 349)
00949849 **Image available**

POLYNUCLEOTIDES ENCODING TWO NOVEL HUMAN G-PROTEIN COUPLED RECEPTORS, HGPRBMY28 AND HGPRBMY29, AND SPLICE VARIANTS THEREOF

POLYNUCLEOTIDES CODANT DEUX NOUVEAUX RECEPTEURS COUPLES AUX PROTEINES G, HGPRBMY28 ET HGPRBMY29, ET LEURS VARIANTS D'EPISSAGE

Publication Language: English
Filing Language: English
Fulltext Availability:
  Detailed Description
  Claims
Fulltext Word Count: 159910
Publication Year: 2002

28/3,K/1 **(Item 1 from file: 349)**
DIALOG(R)File 349:PCT FULLTEXT

00906328 **Image available**

ULTRASOUND THERAPY
THERAPIE A ULTRASONS

Patent Applicant/Assignee:
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Patent Applicant/Inventor:
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MICHALE Anthony Patrick, Gendel Limited, Science Business Incubator Unit, Cromore Road, Coleraine, County Londonderry BT52 1RF, GB, GB (Residence), IE (Nationality), (Designated only for: US)
ROLLAN-HARO Ana Maria, Gendel Limited, Science Business Incubator Unit, Cromore Road, Coleraine, County Londonderry BT52 1RF, GB, GB (Residence), ES (Nationality), (Designated only for: US)
Legal Representative:
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Patent and Priority Information (Country, Number, Date):
Patent: WO 200240093 A2 20020523 (WO 0240093)
Application: WO 2001GB5065 20011116 (PCT/WO GB0105065)
Priority Application: GB 200028121 20001117; GB 20015643 20010307; US 2001279812 20010329; GB 200120582 20010823; US 2001322388 20010914
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 21575

Main International Patent Class: **A61N-001/00**
Fulltext Availability:
Detailed Description

Detailed Description
... ultrasound (either focussed or non-focussed) It has been found that delivery of short, intense **electric pulses** to cell populations or tissues (in vivo) results in transient permeabilisation and this has provided...

...impermeable to those drugs. It has since been developed to a stage where delivery of **electric pulses** in vivo is being exploited in areas such as gene therapy in order to mediate...

...More recently it has been found that exposure of human erythrocytes to short and intense **electric pulses** which facilitates transient permeabilisation also results in a dramatic sensitisation to low intensity ultrasound (WO...A) and electro-sensitised (0) 707 cells in suspension. Cells are electrosensitised by treatment with **electric pulses** of 3.625kV/cm at 1 @tF and cell viability is deten-nined immediately following...8 (*) hours after 1 5 electrosensitisation. Control populations consisted of untreated (N) or treated with **electric pulses** (X) or ultrasound (0) alone. In these experiments error bars represent +SEM where nFigure 9...

...is a graph showing sensitisation of tumours to ultrasound using

highintensity, short-duration square wave **electric pulses** . Each group consists of 4 animals and each group is treated with **electric pulses** alone (0), ultrasound alone (A), electric field treatment followed 24 hours later by ultrasound (T...to, administration of the disrupter, for example, the ultrasound. However, unlike methods for in vivo **electroporation** of the prior art, the present invention is not primarily concerned with the modification of...

...field energy is preferably administered substantially as described in the art, using one or more **electric pulses** of from about I Volt/cm to about 1 0 kVolts/cm under in vivo...

...addition to the pulses, the electric field may be delivered in a continuous manner. The **electric pulse** may be applied for between I @ts and 5 00 milliseconds, preferably between ...Electrosensitisation typically occurs in the absence of an agent to be loaded into the cell. **Electroporation** , which facilitates passage of agents into the cell, occurs in the 0 presence of an...or otherwise, and may vary in strength and/or direction in a time dependent manner.

Electroporation has been used in both in vitro and in vivo procedures to introduce foreign material...

...an electrical field to the cell/implant mixture. Examples of systems that perform in vitro **electroporation** include the Electro Cell Manipulator ECM600 product, and the Electro Square Porator T820, both made by the BTX Division of Genetronics, Inc (see US Patent No 5869326).

The known **electroporation** techniques (both in vitro and in vivo) function by applying a brief **high voltage pulse** to electrodes positioned around the treatment region.

The electric field generated between the electrodes causes...

...porous, whereupon molecules of the agent of interest enter the cells.

1 0 In known **electroporation** applications, this electric field comprises a single square wave pulse on the order of I...

...T820.

Electrosensitisation may be perfonned in a manner substantially identical to the procedure followed for **electroporation** , with the exception that the electric field is 1 5 delivered in the absence of...

...be carried out at different electric field strengths (and other parameters) from those required
for **electroporation** . For example, lower field strengths may be used for electrosensitisation. Thus, systems for **electroporation** may be used for delivery of electric fields to cells, tissues, etc, in the methods...

...varying strength and/or capacitance. As used herein, the term "pulse" includes one or more **electric pulses** at variable capacitance and voltage and including exponential and/or square wave and/or modulated wave/square wave forms.

Preferably the **electric pulse** is delivered as a waveform selected from an exponential wave form, a square wave form...apoptosis. Apoptosis may be assayed as described below. Thus, a high intensity, short duration exponential **electric pulse** may be employed, for example, for apoptosis.

The term "high intensity" should be taken to...

...nis or 450 ms. For example, we disclose the use of a single or multiple **electric pulse** at 1.33 kV/cm, applied for between about 250 ms to 450 ms, in...with corticosteroids, calcipotrine, coal tar preparations, a

systemic treatment with methotrexate, retinoids, cyclosporin A and **photochemotherapy** . The combined treatment is especially important for treatment of an acute or a severe skin...

...or degree of apoptosis is observed to identify molecules which are capable of enhancing, promoting, **inhibiting** or **stopping apoptosis** of the **cells** . Molecules identified by such an assay are useful as drugs to enhance or inhibit apoptotic...

...1.065 X 107 cells/ml. 0.7ml aliquots of this suspension are dispensed into **electroporation** cuvettes (0.4cm electrode gap) together with O. I ml of PBS.

Cuvettes are retained on ice and **electroporated** by delivering two pulses of 3.625kV/cm at a capacitance of 1 VtF. Cells...

...hour. A control population of cells is taken through the same procedure except that the **electroporation** step is omitted. Cell concentrations are adjusted to 1.4 x1 07 Cel,S/ml 107 cells/ml in PBS/Mg) are dispensed into **electroporation** cuvettes (0.4cm electrode gap) together with 0. I ml of PBS. Cuvettes are retained at room temperature and **electroporated** as described for Example I except that one population is treated with two pulses at...
...blue. A control population of cells is taken through the above treatment except that the **electroporation** event is omitted.

The effect of low intensity ultrasound on cells treated at both voltages ...

...the control population. Ultrasound-mediated effects are observed in the population of cells treated with **electric pulses** of 1.875kV/cm and viability is decreased at the lower ultrasound densities (0.25...

...The results confirmed that ultrasound sensitivity could be induced by exposure of cell populations to **electric pulses** . The results also demonstrate that susceptibility of cells to ultrasound increased with increasing electric field...

...it was decided to embed the cells in an alginate matrix, expose the mass to **electric pulses** and subsequently expose it to ultrasound. Viability could then be determined using a modification of...

...d) retained in CaC12 for 15min. Beads are subsequently rinsed in PBS and dispensed into **electroporation** euvettes (30 beads /cuvette) together with 0.5ml PBS. Two **electric pulses** of 2.5kV/cm at a capacitance of 1 @& are delivered to each cuvette and...

...consisted of immobilised cells taken through the procedure with the exception of exposure to either **electric pulses** or ultrasound.

The results from these experiments are shown in Figure 3 and they demonstrate...

...had a very limited effect on control cells which had not been exposed to the **electric pulses** . Exposure of cells to **electric pulses** in the absence of ultrasound treatment resulted in a 50% decrease in viability. However, treatment...

...results presented here demonstrate that a mass of cells may be sensitised to ultrasound using **electric pulses** and suggests that this may also be the case in a tissue mass in vivo...versus 84 j/CM2 for continuous wave ultrasound).

These results demonstrate that tumours treated with **electric pulses** in vivo are rendered sensitive to relatively low intensity ultrasound.

Example 6. Sensitisation of Tumour Cells to Ultrasound in vivo Using

Square Wave
Electric Pulses
This Example demonstrates the ability of high intensity and short duration square wave **electric pulses** to sensitise tumour cells to ultrasound in vivo.

In the above series of experiments is...

...field is delivered to the tissues includes both high-intensity, short I 0 duration exponential **electric pulses** and low intensity direct current for a prolonged period of time.

In order to determine...versus 150 j/CM2 for continuous wave ultrasound.

These results demonstrate that turnours treated with **electric pulses** in vivo are rendered sensitive to higher intensities of ultrasound.

Example 8. Treatment of Electrosensitised...

...at a concentration of 1.53xl 06 Cells/ml. 0.8ml aliquots are dispensed into **electroporation** cuvettes (0.4cm electrode gap) and cells are treated with single **electric pulses** at a capacitance of I @ff. Cells are harvested from euvettes and each 0.8ml...

...of a 24-well tissue culture plate. Control populations of cells are not treated with **electric pulses** but are dispensed into 2ml wells. All samples are treated with ultrasound for 30 seconds...

...induced in C3H mice and these are employed as target tumours for combined treatments with **electric pulses** followed by ultrasound.

Control animals receive no treatment. Conditions used in electrosensitisation involve treatment with...it is demonstrated that treating turnours with ultrasound at extended times after delivery of the **electric pulses** yields an increased effect in terms of retarding tumour growth. In order to determine whether...

31/3,K/1 **(Item 1 from file: 349)**
DIALOG(R)File 349:PCT FULLTEXT

00955524
MEDICAL DEVICE
DISPOSITIF MEDICAL
Patent Applicant/Assignee:
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Patent Applicant/Inventor:
LAHTINEN Mika, Tryffelvagen 14, S-756 46 Uppsala, SE, SE (Residence), SE (Nationality), (Designated only for: US)
LAUKANEN Mikko, -, FI (Residence), FI (Nationality), (Designated only for: US)
YLA-HERTTUALA Seppo, Ruukinpolku 7, FIN-70910 Vuorela, FI, FI (Residence), FI (Nationality), (Designated only for: US)
LEPPANEN Olli-Pekka, Ostra Agatan 51 B, S-753 22 Uppsala, SE, SE (Residence), SE (Nationality), (Designated only for: US)
Legal Representative:
STROM & GULLIKSSON IP AB (agent), Sjoporten 4, S-417 64 Goteborg, SE,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200287610 A1 20021107 (WO 0287610)
Application: WO 2002SE848 20020430 (PCT/WO SE0200848)
Priority Application: FI 2001898 20010430
Designated States: AE AG AL AM AT (utility model) AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ (utility model) CZ DE (utility model) DE DK (utility model) DK DM DZ EC EE (utility model) EE ES FI (utility model) FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK (utility model) SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW (EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG (AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW (EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 29157

Fulltext Availability:
Claims

Claim
... the inner surface of blood vessels, heart and lymphatics. "Endothelialisation" is here referred to the **growth** of endothelial **cells** on all mammalian tissue or fluid contacting surfaces of a biornaterial, that is used to the phrase "capillary endothelialisation", to refer to the **growth** of endothelial **cells** on substantially all tissue contacting surfaces of a biomaterial, that is used to form a...

...otherwise specified. "Angiogenesis" and reflections thereof, such as "angiogenic", are here referred to formation and **growth** of endothelial **cells** in the existing mammalian tissue, such as in the surrounding tissue. A translational or a...5,830,430, U.S. 5,770,220), and the traditional physical methods are microinjection, **electroporation** (U.S. 5,304,120), **iontophoresis** , a combination of **iontophoresis** and **electroporation** (U.S. 5,968,006), ultrasound and pressure (U.S. 5,922,687) (Luo & Saltzman...U.S. 4,355,426). In porous grafts, such as vascular grafts, capillary and endothelial **cell growth** is allowed through pores, and the porosity thereof may be from 0 [Lm to 2000... prosthesis, cardiovascular patch and stent grafts, have a porosity that is high enough to allow **growth** of endothelial **cells** through the pores, and some other cardiovascular implants,
such

as heart valves are non-porous...

31/3,K/2 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00809860
MEDICAL DEVICE
DISPOSITIF MEDICAL
Patent Applicant/Inventor:
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Legal Representative:
GOTEBORGS PATENTBYRA DAHLS AB (agent), P.O. Box 606, S-182 16 Danderyd, SE,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200141674 A1 20010614 (WO 0141674)
Application: WO 2000SE2460 20001207 (PCT/WO SE0002460)
Priority Application: SE 994454 19991207; SE 994747 19991223; SE 2000285 20000131
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 33850

Fulltext Availability:
Claims

Claim
... the inner surface of blood vessels, heart and lymphatics. "Endothelialisation" is here referred to the **growth** of endothelial **cells** on all mammalian tissue or fluid contacting surfaces of a biomaterial, that is used to...

...will be used inter1 0 changeably with the phrase "capillary endothelialisation", to refer to the **growth** of endothelial **cells** on substantially all tissue contacting surfaces of a biomaterial, that is used to form a...

...otherwise specified. "Angiogenesis" and reflections thereof, such as "angiogenic", are here referred to formation and **growth** of endothelial **cells** in the existing mammalian tissue, such as in the surrounding tissue. A translational or a...855,910, 5,830,430, 5,770,220), and the traditional physical methods are microinjection, **electroporation** (5,304,120), **iontophoresis** , a combination of **iontophoresis** and **electroporation** (5,968,006), and pressure (5,922,687) (Rowland). Transfection efficiency can also be improved...

31/3,K/3 (Item 3 from file: 349) duplicate of patent tagged in inventa search results
DIALOG(R)File 349:PCT FULLTEXT

00536877
SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT
SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE
Patent Applicant/Assignee:
GENETRONICS INC,

Inventor(s):
LAMBREVA Maya,
BERG Hermann,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200000250 A1 20000106 (WO 0000250)
Application: WO 99US14202 19990625 (PCT/WO US9914202)
Priority Application: US 9890751 19980626
Designated States: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 9253

Fulltext Availability:
Detailed Description
Claims

English Abstract
The present invention is based on the discovery that **electroporation** of a **photosensitive** agent in a cell and subsequent activation of the agent provides more effective killing of the **electroporated** cell than cells exposed to a **photosensitive** agent alone. The invention provides a method and apparatus for inhibiting **cell growth** or enhancing **cell** death. The method includes providing a **photosensitive** agent to a cell; applying an **electric pulse** to the cell of a sufficient strength and duration to **electroporate** the cell with the **photosensitive** agent; and applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting **cell growth** or enhancing **cell** death.

Detailed Description
... more specifically to an apparatus useful for electropermeation of photosensitive agents and methods for inhibiting **cell growth** or enhancing **cell** death.

BACKGROUND OF THE INVENTION
Photoactivation or Photosensitization is a process in which a photosensitive...undesirable cell 5 proliferation.

In a first embodiment, the invention provides a method for inhibiting **cell growth** or enhancing **cell** death. The method includes providing a photosensitive agent to a cell; applying an **electric pulse** to the cell of a sufficient strength and duration to **electroporate** the cell with the **photosensitive** agent; and applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting **cell growth** or enhancing **cell** death.

In another embodiment, the invention provides a method for treating a cell proliferative disorder...

...i.e. electroincorporation), followed by activation of the agent by light or heat, can inhibit **cell growth** or enhance **cell** death where the activated agent is a photooxidizing agent, for example.

The invention therefore provides methods for inhibiting **cell growth** or for enhancing **cell** death as well as in vivo methods including treating a subject with a cell proliferative disorder. A method of the invention applies an **electric pulse** of a sufficient strength and duration to a cell to introduce a **photosensitive** agent, applies light of an activatable wavelength to the cell to activate the agent, whereby the activated agent inhibits **cell growth** or enhances **cell** death. In one embodiment, a
method of the invention employs a photooxidizing agent which can cause oxidization of components of the **electroporated** cell, such as nucleic acid, thereby inhibiting **cell growth** or enhancing **cell** death. An apparatus for treating a cell proliferative disorder in a subject also is provided that includes an electrode capable of applying an **electric pulse** of sufficient strength and duration to **electroporate** a cell in

the subject, and a light conductor for applying light of an activating wavelength to the **electroporated** cell.

The apparatus and the methods of the invention are advantageous in several respects. The apparatus and methods allow for inhibiting **cell growth** or enhancing **cell** death greater than that produced by treating cells with a **photosensitive** agent alone (i.e. without **electroporation**) or **electroporation** alone (without a **photosensitive** agent), for example. Thus, the invention can employ lower doses of a **photosensitive** agent than is typically used in photooxidizing treatment therapies, 1 5 for example. The invention apparatus and methods are further advantageous when used in combination with other techniques for inhibiting **cell growth** , enhancing **cell** death or for treating cell proliferative disorders. For example, in a method of the invention including heat, the addition of heat promotes or accelerates diffusion of the **photosensitive** agent thereby providing an additive or synergistic effect. As the invention employs **electroporation** and **photosensitive** agents that are non-toxic in the unactivated state, if desired, the invention methods afford exquisite control of inhibiting **cell growth** or enhancing **cell** death of undesirable or hyperproliferative cells while avoiding surrounding healthy cells or tissue. For example, **electroporating** diseased tissue or hyperproliferative cells with a **photosensitive** agent while avoiding **electroporation** of non-diseased tissue or normal cells targets particular tissue or cells for death while ...an amount such that when activated or excited, the activated agent is sufficient for inhibiting **cell growth** or enhancing **cell** death. Such amounts also are considered to be an effective amount for treating a cell ...

...a subject when a desired therapeutic effect is produced, eg., cell proliferation is inhibited, tumor **cell growth** is inhibited, tumor **cell** death is enhanced etc. Thus, an effective amount means an amount of agent that is...

...not be so large as to cause excess adverse side effects resulting from inhibiting normal **cell growth** or enhancing normal **cell** death. The amount required will vary depending on the **photosensitive** agent used, cell type treated, the proliferative disorder treated, the severity of the disorder being treated, the efficiency of cell **electroporation** , the subject treated, the species, age, general condition of the subject and the mode of...

Claim

A method for inhibiting **cell growth** or enhancing **cell** death comprising:

a) providing a photosensitive agent to a cell;

b) applying an **electric pulse** to the cell of a sufficient strength and duration to **electroporate** the cell with the **photosensitive** agent; and

C) applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting **cell growth** or enhancing **cell** death.

2 The method of claim 1, wherein multiple pulses are applied to the cell ...

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METHOD AND APPARATUS FOR REDUCING ELECTROPORATION **-MEDIATED MUSCLE REACTION AND PAIN RESPONSE**
PROCEDE ET APPAREIL PERMETTANT DE REDUIRE LA REACTION MUSCULAIRE INDUITE PAR ELECTROPORATION **ET LA REPONSE DOULOUREUSE**
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METHOD AND APPARATUS FOR REDUCING ELECTROPORATION **-MEDIATED MUSCLE REACTION AND PAIN RESPONSE**
PROCEDE ET APPAREIL PERMETTANT DE REDUIRE LA REACTION MUSCULAIRE INDUITE PAR ELECTROPORATION **ET LA REPONSE DOULOUREUSE**
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METHOD AND APPARATUS FOR REDUCING ELECTROPORATION **-MEDIATED MUSCLE REACTION AND PAIN RESPONSE**
PROCEDE ET APPAREIL PERMETTANT DE REDUIRE LA REACTION MUSCULAIRE INDUITE PAR ELECTROPORATION **ET LA REPONSE DOULOUREUSE**
Main International Patent Class: **A61N-001/00**
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Detailed Description
Claims

English Abstract
This invention is a method for delivery of an agent to a cell using **electroporation** (15) including positioning first, and second electrodes (16) such that an electrical signal passed therebetween...

French Abstract
Un procede permettant d'apporter a une cellule un agent par **electroporation** (15) consiste a positionner des premiere et deuxieme electrodes (16) de sorte qu'un courant...

Detailed Description
METHOD AND APPARATUS FOR REDUCING **ELECTROPORATION** MEDIATED MUSCLE REACTION AND PAIN RESPONSE
FIELD OF THE INVENTION
The present invention relates generally to the use of **electric pulses** to increase the permeability of cell, and more specifically to a method and **electroporation** therapy apparatus for the application of controlled electric fields for delivery of agents into cells by **electroporation** .

BACKGROUND
In the 1970's it was discovered that electric fields could be used to...

...such as pharmacological compounds can be incorporated into live cells through a process known as **electroporation** . The genes or other molecules are mixed with the live cells in a buffer medium...

...genes or molecules enter the cells, where they can modify the genome of the cell.

Electroporation in vivo is often limited to tissue or cells that are close to the skin...
...drug delivery or chemotherapy, such as a tumor, is generally inaccessible to electrodes used for **electroporation** . In the treatment of certain types of cancer with chemotherapy, it is necessary to use...

...drugs, for example, bleomycin, normally cannot penetrate the membranes of certain cancer cells effectively. However, **electroporation** makes it possible to insert bleomycin into cells.

Treatment typically is carried out by injecting an anticancer drug directly into the tumor and applying **electroporation** signals between a pair of electrodes positioned on opposite sides of a tumor. The field strength must be adjusted reasonably accurately so that **electroporation** of the cells of the tumor occurs without damage, or at least minimal damage, to...

...distance between them. The aforementioned parent application discloses a system of electrodes for in vivo **electroporation** wherein the electrodes may be inserted into the tumor. In related U.S. Patent No. 5,273,525, a syringe for injecting molecules and macromolecules for **electroporation** utilizes needles for injection which also function as electrodes. This construction enables subsurface placement of...

...transfer. To overcome this barrier, a novel, non-viral approach, involving the basic concept of **electroporation** to introduce genes into the epidermis or muscle is provided by the present invention.

Treatment of a subject using **electroporation** provides a means for avoiding the deleterious effects typically associated with administration of anticancer or...

...avoiding surrounding healthy cells or tissue.

However, the electrical signals which are typically used for **electroporation** cause considerable discomfort to a patient. There is often enough discomfort that patients are given general anesthesia before receiving the **electroporation** treatment.

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SUMMARY OF THE INVENTION
The present invention is based on the discovery of apparatuses, instruments and methods for reducing pain often associated with clinical use of **electroporation** and delivery of agents to cells. The invention provides such apparatus and instruments which allow administration of **electric pulses** to a patient while reducing the level of discomfort. In one embodiment, a method of...

...treatment site for in vivo delivery of an agent.

The invention also relates to an **electroporation** instrument for use with an **electroporation** therapy apparatus having two or more electrodes. The **electroporation** instrument includes a connector configured to be coupled with the **electroporation** therapy apparatus. The connector provides electrical communication between the **electroporation** instrument and the electrodes of the **electroporation** therapy apparatus.

The **electroporation** instrument also includes electronics for applying an electrical signal to the two or more electrodes...

...has a bipolar square waveforin.

One embodiment of the invention includes electronics for applying an **electroporation** signal to the electrodes of the **electroporation** therapy apparatus and electronics for applying an agent movement signal to the electrodes of the **electroporation** therapy apparatus. The agent movement signals can be applied independently of the **electroporation** signals.

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Another embodiment of the **electroporation** instrument includes electronics tbr applying therapeutic electrical signals to the plurality of electrodes and electronics...

...site in an orientation suitable for applying the therapeutic electrical signals to the electrodes. The **electroporation** instrument can also include electronics for withholding the therapeutic signals if the electrodes are not...

...in an orientation suitable for application of the therapeutic signals.

Yet another embodiment of the **electroporation** instrument includes electronics for applying an electrical signal having a bipolar waveform to the electrodes of the **electroporation** therapy apparatus. The electronics include a power source for producing a monopolar electrical signal and...

...changing electronics for changing the monopolar electrical signal to a bipolar electrical signal. Hence, the **electroporation** instrument can include a single power source for providing bipolar signals.

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BRIEF DESCRIPTION OF THE DRAWINGS
Figure 1 illustrates an **electroporation** system according to the present invention.

Figure 2 is a sideview of a **electroporation** therapy apparatus.

Figure 3 illustrates the electrodes of an **electroporation** therapy apparatus positioned at a treatment site.

Figure 4A illustrates an **electroporation** signal used in prior art **electroporation** treatments.

Figure 4B is a Fourier transform of the **electroporation** signal illustrated in Figure 4A.

Figure 5A illustrates an **electroporation** signal including a bipolar square pulse.

Figure 5B is a Fourier transform of the **electroporation** signal illustrated in Figure 5A.

Figure 6 illustrates a bipolar sinusoidal waveform according to the present invention.

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Figure 7A illustrates an **electroporation** signal including a bipolar pulse sequence.

Figure 7B illustrates a time delay between **electroporation** signals.

Figure 7C illustrates a time delay between different signals where the **electroporation** signals are different from one another.

Figure 71) illustrates a therapeutic signal including an agent movement signal and a **electroporation** signal.

Figure 7E illustrates an **electroporation** signal which provides a net potential during an **electroporation** therapy treatment.

Figure 7F illustrates another embodiment of an **electroporation** signal which provides a net potential during an **electroporation** therapy treatment.

Figure 7G illustrates a net potential which results from terminating an **electroporation** signal without driving the potential of the **electroporation** signal to zero.

Figure 8 is a block diagram of the electronics included in an **electroporation** instrument according to the present invention.

Figure 9 illustrates an embodiment of signal generating electronics for generating bipolar **electroporation** signals. The signal generating electronics includes a single power source.

Figure IO illustrates signal generating electronics for generating **electroporation** signals and/or agent movement signals.

Figure I IA illustrates polarity changing electronics in a...

...polarity changing electronics in a configuration for providing agent movement signals in the absence of **electroporation** signals.

Figure 12A illustrates an embodiment of signal generating electronics including a first power source...

...second polarity configuration.

Figure 13 is a process flow for a method of operating an **electroporation** instrument to provide an **electroporation** treatment.

Figure 14 is a process flow for a method of operating an **electroporation** instrument to test whether an electrode of the **electroporation** therapy apparatus is positioned too close to a metal implement to safely deliver the **electroporation** signals.

Figure 15 is a process flow for a method of operating an **electroporation** instrument to test whether there is sufficient contact between each electrode and the treatment site...

...site.

Figure 16 illustrates experimental results illustrating that an increase in the frequency of the **electroporation** signals according to the present invention reduces the discomfort to the patient.

Figure 17 illustrates the results of treating tumors in mice with **electroporation** therapy according to the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT
The present invention provides an instrument and method for the therapeutic application of **electroporation** . Two or more electrodes are positioned at a treatment site such that a therapeutic electricalThe therapeutic electrical signal can include an **electroporation** signal and/or an agent movement signal. The **electroporation** signal creates pores in the cells located at the treatment site. The agent can then...

...therapeutic electrical signals to the treatment site.

One embodiment of the invention relates to an **electroporation** instrument for use with an **electroporation** therapy apparatus having two or more electrodes for positioning at a treatment site. The **electroporation** instrument includes a connector configured to be coupled with the **electroporation** therapy apparatus. The connector provides electrical communication between the **electroporation** instrument and the electrodes of the **electroporation** therapy apparatus. The **electroporation** instrument I 0 also includes electronics for applying an **electroporation** signal to the two or more electrodes. The **electroporation** signal has a bipolar square waveform and a frequency greater than about 1 0 kHz...

...the frequency of the electrical signal increases. As a result, the 1 5 use of **electroporation** signals having a frequency greater than about 1 0 kHz reduces the level of discomfort to a patient.

In one embodiment of the invention, the **electroporation** signals have a bipolar waveform. In another embodiment, the signals have a bipolar square waveform.

Prior **electroporation** signals have a monopolar square waveform. A Fourier transform of these waveforms shows that the...

...square waveform reduces the discomfort to a patient below what can be achieved with prior **electroporation** signals. This discomfort reduction is further reduced by delivering **electroporation** signals having a bipolar square waveform and a frequency greater than about IO kHz. The...
...electrode corrosion from what results when a monopolar signal is applied.

One aspect of the **electroporation** instrument includes electronics for

testing whether the electrodes are positioned at the treatment site in an orientation suitable for
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applying the **electroporation** signals to the electrodes. For instance, the electronics can test whether the electrodes are positioned too close to a metal implement to safely deliver **electroporation** signals. For instance, if two electrodes are positioned too close to one another, there is a danger of arcing between the electrodes when the **electroporation** signals are applied. As a result, the electrodes would not be positioned in an orientation suitable for application of the **electroporation** signals to the electrodes. The **electroporation** instrument can include electronics for withholding the **electroporation** signals when the electrodes are determined to be positioned in a configuration which is not suitable for application of the **electroporation** signals. As a I 0 result, the **electroporation** instrument increases a patient's comfort level by preventing a patient from experiencing discomfort associated with electrodes being positioned in an orientation which is not suitable for application of the **electroporation** signals.

The **electroporation** system 1 0 includes an **electroporation** instrument 12, a remote controller 14 and an **electroporation** therapy apparatus 15 having a plurality of 1 5 electrodes 16. The **electroporation** instrument 12 includes a connector 18 for coupling the **electroporation** instrument 12 to an **electroporation** therapy apparatus 15. The **electroporation** instrument 12 includes electronics for applying therapeutic electrical signals to the electrodes 16 of the **electroporation** therapy apparatus 15. The therapeutic electrical signals can include **electroporation** signals and/or agent movement signals.

The **electroporation** instrument 12 also includes a remote controller connector 20 for coupling the remote controller 14 with the **electroporation** instrument 12. The remote controller 14 allows a user to control one or more functions of the **electroporation** instrument 12 without touching the **electroporation** instrument 12. A suitable remote controller 14 is a foot pedal switch 22 for activating...

...to the electrode applicator. The foot pedal switch 22 permits a physician to activate the **electroporation** instrument 12 while freeing both hands for positioning of the electrode applicator in a patient's tissue.

The **electroporation** instrument 12 can also include one or more user interfaces 24 for indicating the instrument...

...For instance, the user interfaces can indicate when a fault condition is detected, when the **electroporation**
9
tnerapy is in process, wlien Me **electroporation** tlierapy is complete, and wnen Me **electroporation** instrument is in standby. Suitable user interfaces include, but are not limited to LEDs, displays...

...a readable message and a speakers for providing an audible message.

Figure 2 illustrates an **electroporation** therapy apparatus 15 according to the present invention. The **electroporation** therapy apparatus 15 includes a body 26 and a plurality of electrodes 16. Although three electrodes are illustrated, the **electroporation** therapy apparatus can include as few as two electrodes. An **electroporation** therapy apparatus having more than two electrodes can have the I 0 electrodes 16 positioned
...
...array can be evenly spaced or can have different spacing. Further, an embodiment of the **electroporation** therapy apparatus 15 includes a plurality of electrodes 16 without a body 26. In this **electroporation** therapy apparatus at a treatment site. The tissue piercing distal end aids in penetrating tissues...

...for exemplary electrodes, herein incorporated by reference.

Figure 3 illustrates the electrodes 16 of an **electroporation** therapy apparatus 15 positioned at a treatment site 30 of a patient. The illustrated treatment site 30 includes a tumor 34 which is to receive the **electroporation** treatment. The electrodes 16 are preferably positioned such that therapeutic electrical signals passed between two...

...the cells within the tumor 34 to the therapeutic electrical signal. Correct positioning of the **electroporation** therapy apparatus 15 can include positioning all or a portion of the electrodes 16 on...

...size and accessibility of the treatment site 30.

Although Figure 3 illustrates employment of the **electroporation** therapy apparatus 15 in vivo situation, the **electroporation** therapy apparatuses 14, systems and methods according to the present invention can be similarly employed...

...in a patient and in some embodiments can be an in vitro treatment site.

The **electroporation** instniment 12 includes electronics for applying therapeutic electrical signals to the electrodes 16 of the **electroporation** therapy apparatus 15. As I 0 described above, the therapeutic electrical signals include **electroporation** and/or agent movement signals. The **electroporation** signals serve to temporarily create pores in the cells of the treatment site 30 without...

...can enter the cells within a treatment site 30 through the pores created by the **electroporation** signals.

The agent movement signals cause movement of an agent relative to cells.

Certain agents...

...between cells and the agent, this movement can drive an agent toward a cell. When **electroporation** signals have created pores in the cell, the movement of the agent increases the opportunity...
...the opening. As a result, the agent movement signals can increase the efficiency of an **electroporation** treatment.

Application of electrical signals between the electrodes 16 can cause a patient considerable discomfort...

...the electric field is perceived. One embodiment of the present invention is directed toward applying **electroporation** signals with reduced low frequency components to reduce the discomfort to the patient.

A common **electroporation** signal which is typically used for in-vitro **electroporation** treatments has a monopolar square waveform 36 as illustrated in Figure 4A. Figure 4B shows...

...a large portion of the patient discomfort associated with the monopolar square waveform 36.

The **electroporation** signals according to the present invention preferably have a bipolar square waveform 42 such as...

...not include this low frequency component, the bipolar square waveform reduces the discomfort of the **electroporation** signals.
The **electroporation** signal illustrated in Figure 5A has a first polarity duration 46A and a first polarity peak potential 47A associated with a first polarity 48A.

Additionally, the **electroporation** signal includes a second polarity duration 46B and a second polarity peak potential 47B associated with a second polarity 48B. Although the preferred **electroporation** signal has

a bipolar square waveforin, the present invention is not limited to these waveforms. For instance, suitable **electroporation** signal waveforms include, but are not limited to, monopolar, triangular, circular, 1 2 sinusoidal and...

...duration 46B and a second polarity peak potential 47B of a bipolar sinusoidal waveform.

The **electroporation** signal can include a single bipolar pulse as illustrated in Figure 5A and figure 6 or can include a bipolar pulse sequence as illustrated in Figure 7A. Further, an **electroporation** therapy treatment can include application of several **electroporation** signals separated by a time delay as illustrated in Figures 7B and 7C. The time...

...greater than the time delay of muscle allows the muscle to relax after receiving the **electroporation** signal. Hence, cumulative effects of the **electroporation** signals on the muscle are avoided. The time delay is preferably 0 to 200 ms...

...to 100 ins and most preferably 20 ins to 80 ins. The characteristics of the **electroporation** signal delivered before and after the time delay can be same or can be 1 5 different. For instance, one **electroporation** signal may have a longer duration or a higher peak potential than another **electroporation** signal. Finally, the time delay between different **electroporation** signals can be zero.

The efficiency of delivering an agent to cells can be increased...

...the opportunity for an agent to enter a cell through a pore created by the **electroporation** signals. Because a variety of agents are known to move through a fluid in response...

...movement can be achieved by creating a net potential at a treatment site during an **electroporation** therapy treatment. A net potential means that during application of an **electroporation** signal to a treatment site, the potential applied while the **electroporation** signals is in the first polarity does not offset the potential applied while the **electroporation** signal is in the second polarity. For instance, if the first polarity duration of the...

...within a treatment site. The therapeutic signal includes an agent movement signal combined with an **electroporation** signal. The agent movement signal is a monopolar signal having a substantially constant potential. Hence, the agent movement signal provides a D.C. offset to the **electroporation** signal. The agent movement signal provides a net potential both before, after and during the **electroporation** signal is applied.

Accordingly, movement of the agent is achieved before and after creation of the pores in the cells. Although a single **electroporation** signal is illustrated during application of the agent movement signal, a plurality of **electroporation** signals can be applied I 0 during a single agent movement signal. Further, although the agent movement signal is shown being applied before, after and during the delivery of the **electroporation** signal, the agent movement signal can be applied before and/or after the application of the **electroporation** signal. Figure 7E illustrates an embodiment of an **electroporation** signal which 1 5 provides a net potential. The first polarity peak potential 47A is...

...potential 47B and there is a net potential.

Figure 7F illustrates another embodiment of an **electroporation** signal provides a net potential. The first polarity duration 46A is the same as the...

...components to a bipolar square wave.

Agent movement can be achieved by not driving the **electroporation** to zero potential. Figure 7G illustrates the potential within a treatment site during application of an **electroporation** signal. At the point labeled A, the **electroporation** signal is stopped without driving the potential to zero. The cells within a treatment site have a capacitive effects. Hence, once application of the **electroporation** signal is stopped
14
without driving the potential to zero, the cells discharge leaving the...

...the treatment site and accordingly provides movement of an agent within the treatment site.

Other **electroporation** signals which can provide agent movement include **electroporation** signals where the second polarity duration 46B is different from the first polarity duration 46A...

...47A.

The discomfort to the patient is further reduced by increasing the frequency of the **electroporation** signal. The frequency is related to the first polarity duration 46A I 0 and the...

...Second polarity duration) (1)
The frequency refers to the frequency of the pulses within an **electroporation** signal.

1 5 Since a single **electroporation** treatment can employ different **electroporation** signals, an **electroporation** therapy can include **electroporation** signals having different frequencies.

Experimental data shows that as the frequency of **electroporation** signals
having a bipolar square waveform increases, the patients have an increased tolerance to the...of the invention the pulse duration is about 2 Ps50 Vts.

The efficiency of cell **electroporation** increases as the energy field between the electrodes 16 increases. The energy field created between...

...the electrode centers.

E = V/(2r In (D/r)) (2)
1 0
Delivery of the **electroporation** signals preferably includes creating an energy field of at least about 25 V/cm and...

...at least about 1 00 V/cm between two of the electrodes 16 of the **electroporation** therapy apparatus 15. In one embodiment of the invention, delivery of the **electroporation** signals includes creating an energy field 1 5 of about 1 00 V/cm- IO...

...yet another includes creating an energy field of about I kV/cm-2 Mcm.

The **electroporation** signals preferably are delivered with an energy field of at least about 25 V/cm...

...about I 00 V/cm between at least two of the electrodes 16 of the **electroporation** therapy apparatus 15. In one embodiment of the invention, the energy field during delivery of the **electroporation** signals is about I 00 V/cm- 1 0 Mcm. In another embodiment, the energy field during delivery of the **electroporation** signal is about I kV/cm-3 kV/cm and in another about I kV/cm2 Mcm.

As the electric field increases, the total **electroporation** signal

duration can be decreased in order to prevent excessive amounts of energy from being delivered to the treatment site 30. The total **electroporation** signal duration is the sum of the first polarity durations and the second polarity durations of each **electroporation** signal included in a single **electroporation** therapy treatment. The total **electroporation** signal duration is preferably less than about IO seconds, more preferably about 3 0 [is...

...30 @ts - I ms and most preferably about 50 pts
1 6
ins, When the **electroporation** signals include pulses, the total number of bipolar pulses is preferably I to 1,000...
...achieve these electric fields within treatment sites 30 including tumors 34 having typical dimensions, the **electroporation** signal preferably has a peak potential of less than 1 0 kV, more preferably at...

...V and most preferably at least IO V.

In one embodiment of the invention, the **electroporation** signal has a peak potential of 500 V- IO kV and in another embodiment the **electroporation** signal has a peak potential of about 1 kV-5 kV and in yet another embodiment the **electroporation** signal has a peak potential of about 1 kV-3 W. When the **electroporation** signal has a square waveform, the peak potential is the potential of the signal during the **electrical pulse** .

Figure 8 is a block diagram of electronics 54 included in the **electroporation** instrument 12 according to the present invention. The electronics 54 includes a controller 56 in...

...the one or more processors and/or for storing data developed during operation of the **electroporation** instrument 12. Suitable memories include, but are not limited to, RAM and electronic read-only...
...second output line 72 and distributes the therapeutic signals to the electrodes 16 of the **electroporation** therapy apparatus 15. The controller 56 can operate the relay device 60 to select the...a user interface can be used to indicate this condition to the operator of the **electroporation** instrument 12. Additionally, the signal producing electronics can be temporarily disabled until the operator has...

...user interface 24 can be activated to indicate this condition to the operator of the **electroporation** instrument 12. Additionally, the signal producing electronics can be temporarily disabled until the operator has ...

...any potential but preferably has a potential on the order of the potential of the **electroporation** signals. The current and potential can be measured in order to determine the current through...

...sufficient contact between each of the electrodes 16 and the treatment site 30 and the **electroporation** treatment is allowed to continue.

Although the current is used in the above example of...of the user interfaces such as an LED. This user interface indicates that the
20
electroporation instrument 12 is ready to deliver the therapeutic electrical signals to the treatment site 30...

...source 84 capable of charging the storage device 86 within the time requirements of the **electroporation** instrument 12. The controller 56 can use the crowbar 88 to short the storage device...

...generating electronics 62 of Figure 9 adapted to provide agent movement signals in addition to **electroporation** signals. Agent movement signal generating electronics 62 are tapped into the first bridge line 1...

...signal is a DC signal, the agent movement signal adds a DC offset to the

electroporation signals. The agent movement signal generating electronics can be 1 5 activated before, after or...

...movement signals is preferably about I 00 [ts -1 0 seconds.

During operation of the **electroporation** instrument, the switches of the polarity changing electronics can occupy a variety of different configurations...generating electronics, the agent movement signal can be applied to the electrodes 16 without the **electroporation** signals by using the configuration illustrated in Figure I ID. The second and fourth switches are closed to prevent the flow of the **electroporation** signals. However, the first and third switches are open to permit flow of agent movement signals. Hence, the agent movement signals are applied to the electrodes 16 without the **electroporation** signals. This switch configuration is employed when the agent movement signal is desired without the **electroporation** signal. For instance, this configuration can be employed between delivery of **electroporation** signals in order to encourage an agent to enter the pores opened by the **electroporation** signals.

During operation of the **electroporation** instrument 12, the switches are left in the standby configuration before and after delivery of...

...the first polarity configuration and the second polarity configuration at the desired frequency. When an **electroporation** signal having a first polarity duration 46A which is different than a second polarity duration ...

...and the second I 0 configuration for the second polarity duration 46B. Additionally, when an **electroporation** signal having a first polarity peak potential which is different than a second polarity peak...
...selectively engaged in order to add additional potential to one or more portions of an **electroporation** signal.

1 5 The time delay needed to switch between switch configuration should be taken into account when creating **electroporation** signals having a desired waveform since this time delay can reduce the pulse duration at ...72 is the opposite of what is illustrated in Figure 12C.

During operation of the **electroporation** instrument 12, the switches are left in the standby configuration before and after delivery of the therapeutic electrical signals. To deliver an **electroporation** signal of a single pulse, the switches are transferred to either the first configuration polarity...

...and the second polarity configuration at a frequency which provides the desired waveform. When an **electroporation** signal having a first polarity duration 46A which is different than a second polarity duration ...

...first polarity duration and the second configuration for the second polarity duration. Additionally. when an **electroporation** signal having a first polarity peak potential which is different than a second polarity peak...

...time delay needed to switch between switch configuration should be taken into account when creating **electroporation** signals having a particular waveform since this time delay can reduce the pulse duration at...

...in Figure 12A can be adapted to produce agent movement signals in addition to the **electroporation** signals.

Although Figures 10-12D are directed toward signal generating electronics for
development of **electroporation** signals having bipolar square waveforrns,
embodiments of the invention do not require these signal generating

electronics. For instance, the **electroporation** instrument can include signal generating electronics for I 0 creation of **electroporation** , but not limited to, monopolar, triangular, circular, sinusoidal and exponential.

Figure 13 illustrates a method of operating an **electroporation** instrument 12 according to the present invention. The method begins at start block 300 when an operator indicates to the **electroporation** instrument 12 that the electrodes 16 are in position for delivery of the therapeutic signals...

...an example of a method for making this determination. If the determination is positive, the **electroporation** instrument operator is notified at process block 304. This notification can be provided to the...

...1. For instance, the user interface labeled "READY" can be lit to indicate that the **electroporation** instrument is ready to provide the therapeutic signals. Upon actuation of a remote controller 14...

...illustrated in Figure 13 is for illustrative purposes only and other methods of operating an **electroporation** instrument are within the scope of the invention. For instance, as described above, the ...electrode is positioned too
close to a metal implement. The following description presumes that the **electroporation** instrument includes the signal generating electronics 62 disclosed in Figure 9, however, the method can...

...the electrodes 16. Since the first diagnostic signal preferably has a lower potential than the **electroporation** signals, the storage device 86 is preferably only partially charged. At process block 321 two or more of the electrodes 16 on the **electroporation** apparatus are selected. At process block 322, the first diagnostic signal is applied to the...

...from the electrodes 16 to the treatment site 30. The following description presumes that the **electroporation** instrument includes the signal generating electronics 62 disclosed in Figure 9, however, the method can...two of the one or more electrodes. In one embodiment, the electrical signal includes an **electroporation** signal. In another embodiment, the electrical signal includes an **electroporation** signal and/or an agent movement signal. One embodiment of the method also includes introducing the agent into the proximity of the two or more electrodes.

The **electroporation** signals preferably have a frequency greater than about I 0 kHz, more preferably at least...

...in another about I kV/cm-2 Mcm.

As the electric field increases, the total **electroporation** signal duration can be decreased in order to prevent excessive amounts of energy from being delivered to the treatment site 30. The total **electroporation** signal duration is preferably less than 1 5 about I 0 seconds, more preferably about...

...achieve these electric fields within treatment sites 30 including tumors 34 having typical dimensions, the **electroporation** signal preferably has a potential of less than about 10 kV, more preferably at least...

...and most preferably at least about IO V. In one embodiment of the invention, the **electroporation** signal has a potential of about 5 00 V-I 0 kV and in another embodiment the **electroporation** signal has a potential of about I kV-5 kV and in yet another embodiment the **electroporation** signal has a potential of about I kV-3 W.

As described above, **electroporation** therapy includes introduction of one

or more agents to a subject and delivery of therapeutic...

...antibodies. The term polynucleotides include DNA, cDNA, RNA sequences and complementary sequences thereto.

32
The **electroporation** signals according to the method can have a monopolar
waveform but preferably have a bipolar...appropriate time to 1 5 administer the agent in relation to the administration of the **electric pulse** . For example, while not wanting to be bound by a particular theory, it is believed...

...point (e.g., neocarcinostatin, IEP = 3.78), would likely be more effective if administered post- **electroporation** in order to avoid electrostatic interaction of the highly charged drug within the field. Further...

...into a tumor cell and are typically administered prior to or substantially simultaneous with the **electric pulse** . In addition, certain agents may require modification in order to allow more efficient entry into...

...modified to increase solubility in water which would allow more efficient entry into the cell.

Electroporation facilitates entry of bleomycin or other similar drugs into the tumor cell by creating pores...often the tumor 34 is necrotic. Preferably, the agent is administered substantially contemporaneously with the **electroporation** treatment. The term "substantially contemporaneously" means that
36
the agent and the **electroporation** treatment are administered reasonably close together with respect to time. The administration of the agent...

...subcutaneous cancers. Other cell proliferative disorders, such as warts, are amenable to treatment by the **electroporation** method of the invention. The term "cell proliferative disorder" denotes malignant as well as non...

...also useful for veterinary uses in nonhuman animals or mammals.

37
The advantages offered by **electroporation** for skin and muscle-directed gene therapy and vaccination include: (1) elimination of the risk...

...the CpG-containing oligonucleotide and an antigen or antigen-encoding nucleic acid molecule and the **electroporation** treatment are administered reasonably close together with respect to time. The administration of the adjuvant...
...interval. depending upon such factors, for example, as the nature of the tissue to be **electroporated** , the condition of the patient, the size and chemical characteristics of the antigen and half...and/or muscle, preferably human, by contacting the skin with nucleic acid and applying an **electrical pulse** to the targeted region. The **electrical pulse** is of sufficient voltage and duration to cause **electroporation** so that the antigen or antigenencoding nucleic acid molecule can penetrate into the cells of...

...invention, the molecules to be introduced are topically applied. It should be understood that the **electroporation** of tissue can be
39
pertormed in vitro, in vivo, or ex vivo. **Electroporation** can also be performed utilizing single cells, e.g., single cell suspensions or in vitro...of penetration, the target tissue type, and the like, it may be desirable to conduct **electroporation** in combination with other electrically-based treatment modalities.

Electropulsing conducted substantially contemporaneously with **iontophoresis** (IPH), can produce a greater therapeutic effect than either applying the pulse or **iontophoresis** alone. Furthermore, electroincorporation (El) (see, e.g., US Patent No. 5,464,386, which is ...

...embodiment of the present invention, electropulsing is used in conjunction with one or more of **iontophoresis** and electroincorporation.

As used herein, the term "transdermally introducing" and grammatical variations thereof, refers to...

...the composition to the target tissue prior to, substantially contemporaneously with, or after applying an **electric pulse** , **iontophoresis** , vibration or ultrasound, in their various embodiments.

Depending on the specific formulation, a composition can...

...manner.

45
As used in the above context, the term "substantially contemporaneously" means that the **electric pulse** and the composition are applied to the skin reasonably close together in time. Preferably, the...

...be administered before or after each of the pulses, or at any time between the **electrical pulses** . When applying any auxiliary electrically-based therapy (i.e., IPH, El, and the like), vibration...

...timing of the QRS complexes should appear not to differ during the train of the **electroporation** pulses, and no clinical disturbances of the cardiac rhythm should be observed. Administration of an...

...a graft with autologous or heterologous tissue, the cells in the tissue can be
46
electroporated , ex vivo, with a nucleic acid encoding a protein of interest. Since **electroporation** is relatively fast, a desired nucleic acid can be transferred in a saphenous vein, e...a scaffolding where appropriate cells containing a nucleic acid sequence of interest that has been **electroporated** , ex vivo, can be seeded.

The method of the invention can be used to treat...

...proliferation and migration, platelet
aggregation and extracellular modeling is also desirable for use in the **electroporationmediated** delivery method of the invention. Such compositions include interferon.gamma. which inhibits proliferation and expression...

...may alternatively be used.

EXAMPLES
Example 1
Six volunteers were each exposed to four different **electroporation** signals.

Each **electroporation** signal had a bipolar square waveform and a different frequency.

The volunteers were asked to...

...0 meant no pain and I 0 was unbearable. The responses related to the same **electroporation** signals were averaged. Figure 15 plots the averaged discomfort level versus the frequency of the **electroporation** signals. Increasing the signal frequency 1 5 more than halved the

discomfort level.

Example 2...
...hrs in a 5% CO 2- air atmosphere at 37C before carrying out the XTT **cell survival** assay that is based on metabolic conversion of 48
tetrazolium salts to formazan which is...

...measured spectrophotometrically at 450 rim. using a microplate reader (Packard, Model Spectra Count). The percent **cell survival** values are relative values calculated from the O.D.

values of the sample, [ODsampleb control with 100% **cell survival** (D-E-), [OD I OO], and control with 0% **cell survival** (D-E- with SDS), [ODO], using the formula.

% **cell survival** =([ODsample] - [ODO]) / ([OD I 00] - [ODO]) x I 00
I 0 Typical results showed that...

...lapse of IO +/- I minute was maintained between the drug injection and the application of **electric pulse** to allow bleomycin to spread uniformly throughout the tumor 34. The **electrical pulses** , generated by the prototype bipolar square wave pulse generator, were delivered to the tumor 34...tumor cells histopathologically.
Figure 16 illustrates the results for the experimental and control groups. The **Electroporation** therapy of HEp-2 resulted in a severe early edema, and later necrosis of the...

Claim
... of claim 1, wherein passing one or more electrical signal includes passing a plurality of **electroporation** signals between the two or more electrodes with a time delay of about 0 to 200 ins between the **electroporation** signals.

6 The method of claim 1, wherein the one or more electrical signals have ...

...method of claim 1, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of less than about IO seconds.

16 The method of claim 1, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of about I ms to I 0 seconds.
52
. The method of claim 1, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of about 30 @ts to I milliseconds.
18 The method...

...of claim 24, wherein passing one or more electrical signals includes passing a plurality of **electroporation** signals between the two or more electrodes with a time delay of about 0 to 200 ms between the **electroporation** signals.

29 The method of claim 24, wherein the one or more electrical signals have...method of claim 24, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of less than about IO seconds.

39 The method of claim 24, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of about I ms to IO seconds.

40 The method of claim 24, wherein the one or more electrical signals includes a plurality of **electrical pulses** having a total pulse duration of about 30 @Ls to I milliseconds.

5 5
. The...
...vitro.

50 The method of claim 24, wherein the delivery is ex vivo.

51 An **electroporation** instrument for use with an **electroporation** therapy
apparatus having two or more electrodes, comprising:
a connector configured to be coupled with the **electroporation** therapy apparatus so as to provide electrical communication between the **electroporation** instrument and the electrodes of the **electroporation** therapy apparatus; and electronics for applying one or more electrical signal to the two or...

...5 1, wherein passing the one or more electrical signals includes passing a plurality of **electroporation** signals between the two or more electrodes with a time delay of about 0 to 200 ins between the **electroporation** signals.

56 The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals have a frequency greater than about 40 kHz.
5 7
. The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals have a frequency of about 40 kHz to I 0 MHz.

58 The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals have a frequency less than about IO MHz.

59 The **electroporation** instrument of claim 5 1, further comprising:
electronics for creating an electric field of at least about 25 V/cm between the electrodes.
I 0

60 The **electroporation** instrument of claim 5 1, further comprising:
electronics for creating an electrical field of about 25 V/cin - 500 V/cm.
between the electrodes,
1 5 61. The **electroporation** instrument of claim 5 1, further comprising:
electronics for creating an electric field of about 25 V/cm- ,I 0,000 V/cm between the electrodes.

62 The **electroporation** instrument of claim 5 1, further comprising:
electronics for creating an electric field of about...
...I 0,000 V/cm between the first electrode and the second electrode.

63 The **electroporation** instrument of claim 5 1, wherein the ...signals have a potential greater than about I 0 V between the electrodes.

64 The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals have a potential less than about I 0,000 V between the electrodes.

65 The **electroporation** instrument of claim 5 1, wherein the one or more electrical 3 0 signals include a plurality of **electrical pulses** having a total pulse duration of less than about 10 seconds.
5 8
. The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals include a plurality of **electrical pulses** having a total pulse duration of about I ms to 1 0 seconds.

67 The **electroporation** instrument of claim 5 1, wherein the one or more electrical signals include a plurality of **electrical pulses** having a total pulse duration of about 30 @ts to I milliseconds.

68 The **electroporation** instrument of claim 5 1, wherein the one or more

electrical 1 0 signals include two or more **electrical pulses** having opposite polarities.

69 An **electroporation** therapy system, comprising:
an **electroporation** therapy apparatus having two or more electrodes; and electronics for applying one or more electrical...

...69, wherein the one or more electrical signals have a bipolar square waveform.

71 A **electroporation** instrument for use with an **electroporation** therapy apparatus
having a plurality of electrodes, comprising:
a connector configured to be coupled with the **electroporation** therapy apparatus so as to provide electrical communication between the **electroporation** instrument and the electrodes of the **electroporation** therapy apparatus; and electronics for applying an **electroporation** signal to the electrodes of the
electroporation therapy apparatus; and
electronics for applying an agent movement signal to the electrodes of the **electroporation** therapy apparatus.
3 0
5 9
. The **electroporation** instrument of claim 71, wherein the agent movement
signal can be applied to the electrodes concurrently with the **electroporation** signal.

73 The **electroporation** instrument of claim 71, wherein the agent movement signal can be applied independent of the **electroporation** signals.

74 The **electroporation** instrument of claim 7 1, wherein the agent movement signal adds a DC offset to the **electroporation** signal.

75 The **electroporation** instrument of claim 71, wherein the agent movement I 0 signal is a monopolar signal.

76 The **electroporation** instrument of claim 71, wherein the agent movement signal has a voltage less than about 200 V. 1 5 77. The **electroporation** instrument of claim 71, wherein the **electroporation** signal has a bipolar waveform and a frequency greater than about I 0 kHz.

78 The **electroporation** instrument of claim 77, wherein the bipolar waveform is a bipolar square waveform.

79 The **electroporation** instrument of claim 7 1, wherein the electronics for applying the **electroporation** signal include a first power source in communication with polarity switching electronics and the electronics...

...include a second power source connected in series with the first power source.

80 The **electroporation** instrument of claim 79, wherein the first power source and the second power source are each a DC power source.
60
. A **electroporation** instrument for use with an **electroporation** therapy apparatus
having a plurality of electrodes, comprising:
a connector configured to be coupled with the **electroporation** therapy apparatus so as to provide electrical communication between the **electroporation** instrument and the electrodes of the **electroporation** therapy apparatus; and electronics for applying an electrical signal having a bipolar waveform to the electrodes of the **electroporation** therapy apparatus, the electronics including
a power source for producing a monopolar electrical signal, and...
...for changing the monopolar electrical

I 0 signal to a bipolar electrical signal.

82 The **electroporation** instrument of claim 8 1, wherein the polarity changing electronics include a plurality of switches. 5 83. The **electroporation** instrument of claim 8 1, wherein the polarity changing electronics include a first pair of switches and a second pair of switches arranged in a bipolar H-Bridge.

84 The **electroporation** instrument of claim 8 1, wherein a first power line and a second power line...

...and a second output line connect the polarity changing electronics to the connector.

85 The **electroporation** instrument of claim 84, wherein the polarity changing electronics include a plurality of switches configured...

...second output line and the second power line to the first output line.
61
. The **electroporation** instrument of claim 85, further comprising:
a controller for moving the switches between the first configuration and the second configuration.

87 The **electroporation** instrument of claim 8 1, further comprising:
a DC power source for adding a DC offset to the bipolar signal.

88 The **electroporation** instrument of claim 8 1, further comprising:
a controller for controlling the frequency of the bipolar signal.
I 0

89 The **electroporation** instrument of claim 8 1, further comprising:
a crowbar for shorting the power supply in response to detection of a fault condition. 5 90. The **electroporation** instrument of claim 8 1, wherein the power source includes a plurality of storage capacitors.

91 The **electroporation** instrument of claim 8 1, further comprising:
a power supply connected to the storage capacitors.

92 The **electroporation** instrument of claim 8 1, further comprising:
electronics for monitoring the voltage of the bipolar signal.

93 The **electroporation** instrument of claim 8 1, wherein the electrodes receive the bipolar signal from the polarity changing electronics.
94 The **electroporation** instrument of claim 8 1, wherein the bipolar electrical signal is a bipolar square wave.

95 The **electroporation** instrument of claim 94, further comprising:
a controller for controlling the frequency of the bipolar signal.
62
. The **electroporation** instrument of 8 1, wherein the bipolar signal has a frequency greater than about 1 0 kHz.

97 A **electroporation** instrument for use with an **electroporation** therapy apparatus including a plurality of electrodes for positioning at a treatment site, comprising:
a connector configured to be coupled with the **electroporation** therapy apparatus so as to provide electrical communication between the **electroporation**
instrument and the electrodes of the **electroporation** therapy apparatus;
electronics for applying therapeutic electrical signals to the plurality of
I 0 electrodes...

...in an orientation suitable for applying the therapeutic electrical signals to the electrodes.
98 The **electroporation** instrument of claim 97, further comprising:
electronics for applying therapeutic electrical signals to the plurality

...

...in an orientation suitable for applying the therapeutic electrical signals to the electrodes.

99 The **electroporation** instrument of claim 97, further comprising: electronics for indicating to a user of the **electroporation** instrument that the electrodes are not positioned in an orientation suitable for applying the therapeutic electrical signals to the electrodes. 100. The **electroporation** instrument of claim 97, wherein testing whether the electrodes are positioned in an orientation suitable...

...the electrodes is suitable for applying the therapeutic electrical signals to the electrodes.
63
. The **electroporation** instrument of claim 1 00, wherein testing whether the electrodes are positioned in an orientation...

...the electrodes during the application of the therapeutic electrical signals to the electrodes. 102. The **electroporation** instrument of claim 97, wherein testing whether the electrodes are positioned in an orientation suitable...

...displacement between one or more of the electrodes and an metal implement. 1 03. The **electroporation** instrument of claim 97, wherein electronics for testing whether the electrodes are positioned in an...

...between the electrodes, and
electronics for comparing the measured characteristic to a criterion. 104. The **electroporation** instrument of claim 103, wherein comparing the measured characteristic to a criterion indicates whether the electrodes are too close to one another. 105. The **electroporation** instrument of claim 103, wherein comparing the measured characteristic to a criterion indicates whether at least one electrode is too close to a metal implement.
64
. The **electroporation** instrument of claim 103, wherein the measured characteristic is selected from a group consisting of...

...test signal through the treatment site and power dissipation of the test signal. 107. The **electroporation** instrument of claim 103, wherein the criterion is a threshold value of the measured characteristic. 108. The **electroporation** instrument of claim 103, wherein the criterion is a resistance threshold.
109. The **electroporation** instrument of claim 103, wherein the measured characteristic is a resistance and comparing the measured...

...to a criterion includes comparing the resistance to a resistance threshold.
1 5
110. The **electroporation** instrument of claim 103, wherein the potential of test signal is less than the potential of the therapeutic electrical signals.
111. The **electroporation** instrument of claim I 10, further comprising: electronics for applying therapeutic electrical signals to the...

...that the resistance to the test signal is greater than the resistance threshold.
112. The **electroporation** instrument of claim 103, further comprising:
C@
electronics for indicating to a user of the **electroporation** instrument that the resistance is less than the resistance threshold. 113. The **electroporation** instrument of claim 103, wherein comparing the measured characteristic to a criterion indicates whether a...
...conduction of the therapeutic electrical signals between each electrode and the treatment site.
65

. The **electroporation** instrument of claim 1 1 3, wherein the criterion is a current threshold.
115. The **electroporation** instrument of claim 1 1 3, wherein the measured
characteristic is a current of the...

...measured characteristic to a criterion includes comparing the current to a current threshold.
116. The **electroporation** instrument of claim II 5, further comprising: electronics for applying the therapeutic electrical signals to...

...the test signal through the treatment site is greater than the current threshold.
117. The **electroporation** instrument of claim II 5, further comprising: electronics for indicating to a user of the **electroporation** instrument that the current of the test signal through the treatment site is greater than the current threshold. 118. The **electroporation** instrument of claim 96, wherein the therapeutic electrical signals have a bipolar square waveform. 119. The **electroporation** instrument of claim 96, wherein the therapeutic electrical signals have a frequency greater than about IO kHz.
120. A system for **electroporation** , comprising:
an **electroporation** therapy apparatus including a plurality of electrodes; electronics for applying therapeutic electrical signals to the...international search (name of data base and, where practicable, search terms used)
EAST
Search Terms: **electroporation**
C. DOCUMENTS CONSIDERED TO BE RELEVANT
Category* Citation of document, with indication, where appropriate, of...

35/3,AB/1 (Item 1 from file: 349) a duplicate
DIALOG(R)File 349:PCT FULLTEXT

00536877

SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT

SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE

Patent Applicant/Assignee:
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BERG Hermann,

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Priority Application: US 9890751 19980626
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English Abstract

The present invention is based on the discovery that **electroporation** of a **photosensitive** agent in a cell and subsequent activation of the agent provides more effective killing of the **electroporated** cell than cells exposed to a **photosensitive** agent alone. The invention provides a method and apparatus for inhibiting **cell growth** or enhancing **cell** death. The method includes providing a **photosensitive** agent to a cell; applying an **electric pulse** to the cell of a sufficient strength and duration to **electroporate** the cell with the **photosensitive** agent; and applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting **cell growth** or enhancing **cell** death.

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File 350:Derwent WPIX 1963-2002/UD,UM &UP=200303
         (c) 2003  Thomson Derwent
File 344:Chinese Patents Abs Aug 1985-2002/Nov
         (c) 2002 European Patent Office
File 347:JAPIO Oct 1976-2002/Sep(Updated 030102)
         (c) 2003 JPO & JAPIO
File 371:French Patents 1961-2002/BOPI 200209
         (c) 2002 INPI.  All rts. reserv.

Set     Items   Description
S1     505997   CELL? ?
S2       8831   SURVIV?
S3     205212   DEATH OR DIE OR DIES OR DIED OR DYING
S4     150205   GROWTH
S5     264109   INHIBIT???
S6     707286   STOP? ? OR STOPP???
S7       4243   AVERT???
S8     227094   CHECK???
S9       1946   CURB???
S10      3315   APOPTOSIS
S11       984   S1(2N)S2
S12      2171   S1(3N)S3
S13      3207   S1(2N)S4(3N)S5:S9
S14      6029   S11:S13
S15      1441   ELECTROPORAT?
S16     10087   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17         7   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
             NOTHERAPY OR ION()MEDICATION? ?
S18       730   IONTOPHORESIS
S19     12144   S15:S18
S20    244193   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21      1508   PHOTODYNAMIC()THERAPY OR PDT
S22        72   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    245560   S20:S22
S24         1   S14 AND S19 AND S23
S25   1448258   LASER OR LIGHT
S26         1   (S10 OR S14) AND S19 AND S23 AND S25
S27         0   S26 NOT S24
```

26/3,K/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

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WPI Acc No: 2000-160643/200014
XRAM Acc No: C00-050133
XRPX Acc No: N00-119880

Inhibiting cell growth or enhancing cell death by electroporation of a photosensitive agent in a cell and photo-activation of the agent, useful for treating cancers and tumors

Patent Assignee: GENETRONICS INC (GENE-N)
Inventor: BERG H; LAMBREVA M
Number of Countries: 022 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200000250	A1	20000106	WO 99US14202	A	19990625	200014	B
AU 9950841	A	20000117	AU 9950841	A	19990625	200026	
EP 1100576	A1	20010523	EP 99935345	A	19990625	200130	
			WO 99US14202	A	19990625		

Priority Applications (No Type Date): US 9890751 P 19980626
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200000250	A1	E	41	A61N-001/00	

Designated States (National): AU CA JP
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AU 9950841	A		A61N-001/00	Based on patent WO 200000250
EP 1100576	A1	E	A61N-001/00	Based on patent WO 200000250

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

Inhibiting cell growth or enhancing cell death by electroporation of a photosensitive agent in a cell and photo-activation of the agent, useful for treating cancers and...

Abstract (Basic):
... **Inhibition** of cell **growth** or enhancement of **cell death** comprises providing a **photosensitive** agent to a cell and applying an **electric pulse** of a sufficient strength and duration to the cell to **electroporate** it with the **photosensitive** agent. **Light** of activatable wavelength is applied to the **cell** , thus activating the agent and **inhibiting** cell **growth** or enhancing **cell death** .
... a cell proliferative disorder in a subject, comprising (a) an electrode capable of applying an **electric pulse** of sufficient strength and duration to **electroporate** a cell in the subject; and (b) a **light** conductor for applying **light** of an activating wavelength to the **electroporated** cell...

...The invention is used for **inhibiting** cell **growth** or enhancing **cell death** . It may also be used for treating a cell proliferative disorder which may be benign...

... **Electroporation** of a **photosensitive** agent in a cell and subsequent activation of the agent provides more effective killing of the **electroporated** cell than cells exposed to a **photosensitive** agent alone. The invention employs lower doses of a **photosensitive** agent than is typically used in photooxidizing treatment therapies. The addition of heat promotes or accelerates diffusion of the **photosensitive** agent, thus providing an additive or synergistic effect. The invented method affords exquisite control of **inhibiting** cell **growth** or enhancing **cell death** of undesirable or hyperproliferative cells while avoiding surrounding healthy cells or tissue, since the invention employs **electroporation** and **photosensitive** agents that are nontoxic in the unactivated state

Technology Focus:

... 0.1-6 kV/cm. Pulse width is 0.1-10 milliseconds. At least one **light** conductor is combined with the electrode. The electrode and the **light** conductor comprise an **electroporation** catheter configuration. The **light** conductor comprises a fiber optic rod comprising optical fibers. It is applied by a tungsten...

...a near ultraviolet lamp. It has a wavelength of 300-950 nm. The amount of **light** applied is 50-1000 J/cm2. It is applied extracorporeally or internally. The method further...

...Preferred **Photosensitive** Agent: The **photosensitive** agent is a photooxidizing agent or a cytostatic agent. It is preferably protoporphyrin IX. The...

...Title Terms: **PHOTOSENSITISER** ;

File 348:EUROPEAN PATENTS 1978-2003/Jan W01
(c) 2003 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030109,UT=20030102
(c) 2003 WIPO/Univentio

Set	Items	Description
S1	406296	CELL? ?
S2	41778	SURVIV?
S3	137095	GROWTH
S4	213092	INHIBIT???
S5	280972	STOP? ? OR STOPP???
S6	4654	AVERT???
S7	154767	CHECK???
S8	2198	CURB???
S9	10466	APOPTOSIS
S10	9399	S1(2N)S2
S11	34639	S1(3N)S3
S12	1916	S1(2N)S4(3N)S5:S9
S13	20981	ELECTROPORAT?
S14	8353	(DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S15	1936	ELECTRIC??()PATCH?? OR IONTOPHORESIS OR IONTOTHERAPY OR IONOTHERAPY OR ION()MEDICATION?
S16	29433	S13:S15
S17	27108	PHOTOSENSITI? OR SENSITI?ER?(5N)PHOTOOXID?
S18	1606	PHOTODYNAMIC()THERAPY OR PDT
S19	202	PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S20	406662	LASER OR LIGHT
S21	28243	S17:S19
S22	31528	DEATH
S23	729477	DIE
S24	203565	DIES
S25	7118	DIED
S26	3649	DYING
S27	15195	S1(2N)S22:S26
S28	10643	S1(3N)S2
S29	10064	S1(2N)S3(3N)S4:S8
S30	29466	S9 OR S27 OR S28 OR S29
S31	406662	LIGHT OR LASER
S32	282	S16 AND S21 AND S20 AND S30
S33	1	S16(S)S21(S)S20(S)S30
S34	17	S20/TI,AB AND S16 AND S21 AND S30
S35	16	S34 NOT S33

33/6/1 (Item 1 from file: 349)
00536877 a duplicate

SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT

SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE

Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 9253
Publication Year: 2000

35/6/1 (Item 1 from file: 349)
00966698 **Image available**
ACCELERATORS FOR INCREASING THE RATE OF FORMATION OF FREE RADICALS AND REACTIVE OXYGEN SPECIES
ACCELERATEURS POUR AUGMENTER LE TAUX DE FORMATION DES RADICAUX LIBRES ET DES ESPECES OXYGENEES RADICALAIRES
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 23448
Publication Year: 2002

35/6/2 (Item 2 from file: 349)
00928659 **Image available**
PHOTODYNAMIC STIMULATION DEVICE AND METHODS
PROCEDES ET DISPOSITIF DE STIMULATION PHOTODYNAMIQUE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10108
Publication Year: 2002

35/6/3 (Item 3 from file: 349)
00920932
ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR
ANTICORPS ANTI-RECEPTEUR DU FACTEUR DE CROISSANCE INSULINOIDE I
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 36706
Publication Year: 2002

35/6/4 (Item 4 from file: 349)
00911642
PHOTOCHEMICAL INTERNALIZATION FOR VIRUS-MEDIATED MOLECULE DELIVERY INTO THE CYOSOL
INTERNALISATION PHOTOCHIMIQUE POUR INTRODUCTION DE MOLECULES DANS LE CYTOSOL PAR DES VECTEURS VIRAUX
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 17729
Publication Year: 2002

35/6/5 (Item 5 from file: 349)
00910373 **Image available**
PHOTOCHEMICAL INTERNALIZATION FOR DELIVERY OF MOLECULES INTO THE CYTOSOL
INTERNALISATION PHOTOCHIMIQUE POUR INTRODUIRE DES MOLECULES DANS LE CYTOSOL
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 19868

Publication Year: 2002

35/6/6 (Item 6 from file: 349)
00885422 **Image available**
SCANNING FLUORESCENCE LIFETIME MICROSCOPE: DIRECTED EVOLUTION
MICROSCOPE DE DETERMINATION DE LA DUREE DE VIE DE FLUORESCENCE A BALAYAGE A INTERFACE INFORMATIQUE UTILISE DANS LES TECHNIQUES D'EVOLUTION DIRIGEE ET METHODES DE STRUCTURATION PHOTO-INDUITE UTILISEES DANS LA SELECTION CELLULAIRE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 13524
Publication Year: 2002

35/6/7 (Item 7 from file: 349)
00837002 **Image available**
COMPOUNDS WITH 5-HT"sub"1A ACTIVITY USEFUL FOR TREATING DISORDERS OF THE OUTER RETINA
COMPOSES A ACTIVITE AGONISTE SUR LE RECEPTEUR 5-HT"sub"1A DESTINES AU TRAITEMENT DES AFFECTIONS DE LA RETINE EXTERNE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 4993
Publication Year: 2001

35/6/8 (Item 8 from file: 349)
00830608
ANTIBODY SPECIFIC FOR THE ED-B DOMAIN OF FIBRONECTIN, CONJUGATES COMPRISING SAID ANTIBODY, AND THEIR USE FOR THE DETECTION AND TREATMENT OF ANGIOGENESIS
ANTICORPS SPECIFIQUE AU DOMAINE ED-B DE LA FIBRONECTINE, CONJUGUES CONTENANT CET ANTICORPS, ET UTILISATION POUR LA DETECTION ET LE TRAITEMENT DE L'ANGIOGENESE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 12956
Publication Year: 2001

35/6/9 (Item 9 from file: 349)
00776920
METHOD OF PREVENTING THE INJURY OR DEATH OF RETINAL CELLS AND TREATING OCULAR DISEASES
PROCEDE DE PREVENTION DE LA DETERIORATION OU DE LA MORT DES CELLULES DE LA RETINE ET DE TRAITEMENT DES TROUBLES OCULAIRES
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 58202
Publication Year: 2001

35/6/10 (Item 10 from file: 349)

00740498 **Image available**
METHOD OF PREVENTING THE DEATH OF RETINAL NEURONS AND TREATING OCULAR DISEASES
TECHNIQUE PERMETTANT DE PREVENIR LA MORT DES NEURONES RETINIENS ET TRAITEMENT DES MALADIES OCULAIRES
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 57322
Publication Year: 2000

35/6/11 (Item 11 from file: 349)
00739696
PHOTODYNAMIC THERAPY **IN COMBINATION WITH** APOPTOSIS **INDUCING FACTORS**
THERAPIE PHOTODYNAMIQUE ASSOCIEE A DES FACTEURS INDUISANT L'APOPTOSE
Publication Language: English
Filing Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 14620
Publication Year: 2000

35/6/12 (Item 12 from file: 349)
00576893 **Image available**
TARGETING OF SEBACEOUS FOLLICLES AS A TREATMENT OF SEBACEOUS GLAND DISORDERS
CIBLAGE DE FOLLICULES SEBACES UTILISE POR TRAITER DES TROUBLES DE LA GLANDE SEBACEE
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 11104
Publication Year: 2000

35/6/13 (Item 13 from file: 349)
00547239
METHODS TO ENHANCE AND CONFINE EXPRESSION OF GENES
TECHNIQUE PROPRE A ACCENTUER ET A CONFINER L'EXPRESSION DE GENES
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 14734
Publication Year: 2000

35/6/14 (Item 14 from file: 349)
00527218
SPECIFIC BINDING MOLECULES FOR SCINTIGRAPHY, CONJUGATES CONTAINING THEM AND THERAPEUTIC METHOD FOR TREATMENT OF ANGIOGENESIS
MOLECULES DE LIAISON SPECIFIQUES POUR SCINTIGRAPHIE, CONJUGUES CONTENANT CES MOLECULES ET TRAITEMENT DE L'ANGIOGENESE
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10797
Publication Year: 1999

35/6/15 (Item 15 from file: 349)
00503479
ENHANCED TRANSPORT USING MEMBRANE DISRUPTIVE AGENTS
AMELIORATION DU TRANSPORT PAR L'UTILISATION D'AGENTS DE RUPTURE DE MEMBRANES
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 13074
Publication Year: 1999

35/6/16 (Item 16 from file: 349)
00324924
TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 4835
Publication Year: 1996
?t35/3,ab/2,11,15,16

35/3,AB/2 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00928659
PHOTODYNAMIC STIMULATION DEVICE AND METHODS
PROCEDES ET DISPOSITIF DE STIMULATION PHOTODYNAMIQUE
Patent Applicant/Assignee:
SORENSEN Svein, Mindeveien 30, N-3717 Skien, NO, NO (Residence), NO (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
LARSEN Eric, P.O. Box 1016, CH-8201 Schaffhausen, CH, CH (Residence), DK (Nationality)
Patent and Priority Information (Country, Number, Date):
Patent: WO 200262420 A1 20020815 (WO 0262420)
Application: WO 2002NO33 20020122 (PCT/WO NO0200033)
Priority Application: NO 2001373 20010122
Designated States: AE AG AL AM AT AT (utility model) AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ CZ (utility model) DE DE (utility model) DK DK (utility model) DM DZ EC EE EE (utility model) ES FI FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SK (utility model) SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 10108

English Abstract
A treatment device which uses a **light** radiation of multiple wavelengths and pulse-shaped electromagnetic fields for the photodynamic stimulation of cells, especially cells of human tissue, and also for the activation and stimulation of **light** sensitive substances (PTD). The device produces energy radiation by the use of semiconductor and/or **laser** diodes, which emit **light** in several separate wavelengths due to a special operation mode and the use of tuneable diodes. The equipment consists of a stand, with which machine applicators are connected via a jointed arm. The stand is freely moveable on wheels and includes a control mechanism whereby the various parameters for therapy can be

adjusted and switched on and off. The stand is also connected to a hand applicator for treatment of small tissue-areas, e.g., acupuncture points. Photodynamic substances are introduced into the tissue with a special hand applicator.

French Abstract

Cette invention a trait a un dispositif utilisant un rayonnement de lumiere a longueurs d'ondes multiples et des champs electromagnetiques pulses destines a la stimulation photodynamique de cellules, notamment des cellules de tissu humain, et a l'activation et a la stimulation de substances sensibles a la lumiere (PTD). Ledit dispositif produit un rayonnement d'energie au moyen de diodes **laser** et/ou semi-conductrices, qui emettent de la lumiere dans plusieurs longueurs d'ondes separees en raison d'un mode de fonctionnement special et au moyen de diodes reglables. Ledit materiel comprend un pied, auquel des applicateurs de machine sont relies par le biais d'un bras articule. Le pied est librement amovible sur roues et comporte un mecanisme de commande, dont on peut adapter et commuter les divers parametres afferents a la therapie. Ledit pied peut etre relie a un applicateur manuel destine au traitement de petites zones tissulaires, par exemple, des points d'acupuncture. On introduit des substances photodynamiques dans le tissu avec un applicateur manuel special.

35/3,AB/11 (Item 11 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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a duplicate

00739696

PHOTODYNAMIC THERAPY **IN COMBINATION WITH** APOPTOSIS **INDUCING FACTORS**
THERAPIE PHOTODYNAMIQUE ASSOCIEE A DES FACTEURS INDUISANT L'APOPTOSE

Patent Applicant/Assignee:
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Patent Applicant/Inventor:
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Legal Representative:
ROBINSON J Christopher, Fetherstonhaugh & Co., Suite 2200, 650 West Georgia Street, Box 11560, Vancouver, British Columbia V6B 4N8, CA

Patent and Priority Information (Country, Number, Date):
Patent: WO 200051638 A1 20000908 (WO 0051638)
Application: WO 2000CA200 20000225 (PCT/WO CA0000200)
Priority Application: US 99121770 19990226

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English
Filing Language: English
Fulltext Word Count: 14620

English Abstract

The invention relates to **photodynamic therapy** (**PDT**) used in combination with **apoptosis** -inducing agents to destroy target cells and tissues. Benefits of such combinations include 1) the ability to use lower doses of **photosensitizers** and/or **light** ; 2) the ability to use

lower doses of **apoptosis** -inducing agents; and 3) the ability to use **apoptosis** -inducing agents against target tissues which are otherwise insensitive to the **apoptosis** -inducing agents.

French Abstract
La presente invention concerne la therapie photodynamique (TPD) utilisee en association a des agents induisant l'apoptose, dans le but de detruire les tissus et les cellules cibles. Les avantages de ces associations consistent en: 1) la possibilite d'utiliser des doses inferieures de photosensibilisants et/ou de lumiere; 2) la possibilite d'utiliser des doses inferieures d'agents induisant l'apoptose; et 3) la possibilite d'utiliser des agents induisant l'apoptose contre des tissus cibles qui sont sinon insensibles aux agents induisant l'apoptose.

35/3,AB/15 (Item 15 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00503479
ENHANCED TRANSPORT USING MEMBRANE DISRUPTIVE AGENTS
AMELIORATION DU TRANSPORT PAR L'UTILISATION D'AGENTS DE RUPTURE DE MEMBRANES
Patent Applicant/Assignee:
UNIVERSITY OF WASHINGTON,
UNIVERSITY OF MASSACHUSETTS,
Inventor(s):
HOFFMAN Allan S,
STAYTON Patrick,
PRESS Oliver,
TIRRELL David,
MURTHY Niren,
LACKEY Chantal,
CRUM Lawrence A,
MOURAD Pierre D,
PORTER Tyrone M,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9934831 A1 19990715
Application: WO 99US122 19990105 (PCT/WO US9900122)
Priority Application: US 9870411 19980105
Designated States: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 13074

English Abstract
Compositions and methods for transport or release of therapeutic and diagnostic agents or metabolites or other analytes from cells, compartments within cells, or through cell layers or barriers are described. The compositions include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compositions include compounds which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes, coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as **light** , electrical stimuli, electromagnetic stimuli, ultrasound, temperature, or combinations thereof. The compounds can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontopheresis, and/or electropheresis can also be used with the disrupting agents.

French Abstract

La presente invention concerne des compostions et des methodes de transport ou de liberation d'agents therapeutiques et diagnostiques ou de metabolites ou autres analytes a partir de cellules, de compartiments cellulaires, ou a travers des couches ou des barrieres cellulaires. Ces compositions contiennent un agent ameliorant le transport a travers les barrieres membranaires et sont generalement administrees en association avec un activateur et/ou une exposition a un stimulus, afin de provoquer une rupture ou pour modifier la permeabilite, le transport ou la liberation. Dans un mode prefere de realisation, ces compositions contiennent des composes qui provoquent la rupture des membranes endosomiques en reaction au faible pH des endosomes, mais qui sont relativement inactives face aux cellules membranaires, couplees directement ou indirectement a un agent therapeutique ou diagnostique. On peut egalement utiliser d'autres agents de rupture, sensibles aux stimuli et/ou aux activateurs autres que le pH, tels que la lumiere, les stimuli electrique, electromagnetique, les ultrasons, la temperature ou une association de ces stimuli. Par ailleurs, on peut coupler ces composes a un agent devant etre administre ou a un ligand formant un complexe avec cet agent, par liaison ionique, covalente ou par liaison H. Les agents a administrer peuvent etre des agents therapeutiques et/ou diagnostiques, les traitements ameliorant l'administration tels que les ultrasons, l'iontophorese, et/ou l'electrophorese pouvant etre egalement utilises avec les agents de rupture.

35/3,AB/16 (Item 16 from file: 349) a duplicate

00324924

TRANSFER OF MOLECULES INTO THE CYTOSOL OF CELLS
TRANSFERT DE MOLECULES DANS LE CYTOSOL CELLULAIRE

Patent Applicant/Assignee:
RADIUMHOSPITALETS FORSKNINGSSTIFTELSE,
BERG Kristian,
SANDVIK Kirsten,
MOAN Johan,
Inventor(s):
BERG Kristian,
SANDVIK Kirsten,
MOAN Johan,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9607432 A1 19960314
Application: WO 95NO149 19950904 (PCT/WO NO9500149)
Priority Application: NO 943327 19940908
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 4835

English Abstract
A method for releasing molecules into the cytosol of cells without killing the majority of the cells by allowing the molecules to be taken up in endosomes, lysosomes or other cell compartments and use **light** activation of **photosensitizing** compounds to rupture the membranes of the endosomes, lysosomes or other cell compartments, is described.

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File 155:MEDLINE(R) 1966-2002/Dec W5
File   5:Biosis Previews(R) 1969-2003/Jan W1
         (c) 2003 BIOSIS
File  73:EMBASE 1974-2003/Jan W1
         (c) 2003 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Jan W1
         (c) 2003 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 144:Pascal 1973-2003/Jan W1
         (c) 2003 INIST/CNRS
File   6:NTIS 1964-2003/Jan W2
         (c) 2003 NTIS, Intl Cpyrght All Rights Res
File   2:INSPEC 1969-2003/Jan W1
         (c) 2003 Institution of Electrical Engineers
File   8:Ei Compendex(R) 1970-2003/Jan W1
         (c) 2003 Elsevier Eng.  Info. Inc.
File  99:Wilson Appl. Sci & Tech Abs 1983-2003/Dec
         (c) 2003 The HW Wilson Co.
File  65:Inside Conferences 1993-2003/Jan W2
         (c) 2003 BLDSC all rts. reserv.
File  94:JICST-EPlus 1985-2003/Nov W1
         (c)2003 Japan Science and Tech Corp(JST)
File  35:Dissertation Abs Online 1861-2003/Dec
         (c) 2003 ProQuest Info&Learning

Set     Items   Description
S1   11861372   CELL? ?
S2    1567834   SURVIV?
S3    1708605   DEATH OR DIE OR DIES OR DIED OR DYING
S4    4591321   GROWTH
S5    4601975   INHIBIT???
S6     297228   STOP? ? OR STOPP???
S7      10574   AVERT???
S8     336946   CHECK???
S9       7364   CURB???
S10    328036   APOPTOSIS
S11    153509   S1(2N)S2
S12    237070   S1(3N)S3
S13     87174   S1(2N)S4(3N)S5:S9
S14    446009   S11:S13
S15     20994   ELECTROPORAT?
S16     14063   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17        36   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18     17303   IONTOPHORESIS
S19     50834   S15:S18
S20    104901   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21     28810   PHOTODYNAMIC()THERAPY OR PDT
S22     14422   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    130855   S20:S22
S24         5   S14 AND S19 AND S23
S25         2   RD (unique items)
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25/6/2 (Item 1 from file: 5)
10837828 BIOSIS NO.: 199799458973
Electric field-enhanced activation of hematoporphyrin derivative: Effects of a human tumour cell line.
1997
?t25/7/1

25/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09319576 97218153 PMID: 9065814
Electric field-enhanced activation of hematoporphyrin derivative: effects on a human tumour cell line.
Ward T; Mooney D; Flynn G; McHale A P
School of Applied Biological and Chemical Sciences, University of Ulster, Coleraine, UK.
Cancer letters (IRELAND) Feb 26 1997, 113 (1-2) p145-51, ISSN 0304-3835 Journal Code: 7600053
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In a recent report we described the effects of combined electroactivation and photoactivation of hematoporphyrin derivative (HPD) on human erythrocytes and established that activation-induced cell lysis was more pronounced when both modes of activation were sequentially applied to the system. Here we demonstrate that electric field-induced activation of HPD-treated HeLa **cells** results in **cell death** . This effect is shown to be dependant on both electric field strength and on HPD concentration. In addition, we demonstrate that exposure of HPD-treated cells to short and intense **electric pulses** prior to photoactivation, results in increased cell mortality. The results confirm our earlier suggestion that HPD may be activated in the presence of an applied electric field. The results further suggest that activation of **photosensitizers** using combined exposure to electric fields and light may play an important role in increasing the efficiency of **photodynamic therapy** (**PDT**) in the treatment of cancer.
Record Date Created: 19970407

```
File  95:TEME-Technology & Management 1989-2003/Dec W5
         (c) 2003 FIZ TECHNIK
File  98:General Sci Abs/Full-Text 1984-2003/Dec
         (c) 2003 The HW Wilson Co.
File   9:Business & Industry(R) Jul/1994-2003/Jan 13
         (c) 2003 Resp. DB Svcs.
File  16:Gale Group PROMT(R) 1990-2003/Jan 14
         (c) 2003 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2003/Jan 13
         (c)2003 The Gale Group
File 621:Gale Group New Prod.Annou.(R) 1985-2003/Jan 13
         (c) 2003 The Gale Group
File 149:TGG Health&Wellness DB(SM) 1976-2003/Dec W5
         (c) 2003 The Gale Group
File 636:Gale Group Newsletter DB(TM) 1987-2003/Jan 14
         (c) 2003 The Gale Group
File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Jan W2
         (c) 2003 ESPICOM Bus.Intell.
File  20:Dialog Global Reporter 1997-2003/Jan 14
         (c) 2003 The Dialog Corp.
File  15:ABI/Inform(R) 1971-2003/Jan 13
         (c) 2003 ProQuest Info&Learning
File  88:Gale Group Business A.R.T.S. 1976-2003/Jan 08
         (c) 2003 The Gale Group
File 442:AMA  Journals 1982-2003/Feb B2
         (c)2003 Amer Med Assn -FARS/DARS apply
File 444:New England Journal of Med. 1985-2003/Jan W2
         (c) 2003 Mass. Med. Soc.

Set     Items   Description
S1    1248932   CELL? ?
S2    1274452   SURVIV?
S3    2890211   DEATH OR DIE OR DIES OR DIED OR DYING
S4    5744214   GROWTH
S5     404394   INHIBIT???
S6    2339332   STOP? ? OR STOPP???
S7     100193   AVERT???
S8    1798640   CHECK???
S9     237184   CURB???
S10     23058   APOPTOSIS
S11      9002   S1(2N)S2
S12     32361   S1(3N)S3
S13      8321   S1(2N)S4(3N)S5:S9
S14     45357   S11:S13
S15      2748   ELECTROPORAT?
S16      3630   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17        23   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18      1150   IONTOPHORESIS
S19      7213   S15:S18
S20     11273   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21    156606   PHOTODYNAMIC()THERAPY OR PDT
S22      1175   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    166981   S20:S22
S24        15   S14 AND S19 AND S23
S25        11   RD (unique items)
S26         6   S25/2003 OR S25/2002 OR S25/2001 OR S25/2000 OR S25/1999
S27         5   S25 NOT S26
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27/6/1 (Item 1 from file: 16)
05517999 Supplier Number: 48362504 (USE FORMAT 7 FOR FULLTEXT)
Genetronics Allowed Method Patent for Oncology Treatment
March 17, 1998
Word Count: 559

27/6/2 (Item 1 from file: 442)
00107713

Long-term Follow-up and Histological Changes of Superficial Nonmelanoma Skin Cancers Treated With Topical <unprintable>-Aminolevulinic Acid Photodynamic Therapy (ARTICLE)
1998;
LINE COUNT: 00495

27/6/3 (Item 2 from file: 442)
00097776

Treatment of Kaposi's Sarcoma (ARTICLE)
1996;
LINE COUNT: 00521

27/6/4 (Item 3 from file: 442)
00097201

Visual Perception Elicited by Electrical Stimulation of Retina in Blind Humans (ARTICLE)
1996;
LINE COUNT: 00602

27/6/5 (Item 4 from file: 442)
00050217

In Vitro Photodynamic Treatment of Normal and Human Papilloma Virus--Transfected Keratinocytes With Photofrin II and Red Light (Article)
1991;
?t27/3,k/1-3,5

27/3,K/1 (Item 1 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)

05517999 Supplier Number: 48362504 (USE FORMAT 7 FOR FULLTEXT)
Genetronics Allowed Method Patent for Oncology Treatment
PR Newswire, p317LATU019
March 17, 1998
Language: English Record Type: Fulltext
Document Type: Newswire; Trade
Word Count: 559

(USE FORMAT 7 FOR FULLTEXT)
TEXT:
Electroporation Mediated Delivery of Drugs and Genes -
... Toronto Stock Exchange: GEB) today announced its patent application for a "method of treatment using **electroporation** -mediated delivery of drugs and genes" has been allowed by the U.S. Patent and...

...enter the cell. The process of temporarily and reversibly permeabilizing the cell membrane is termed **electroporation** , and it allows therapeutic drugs or beneficial genes to gain intracellular access within seconds. **Electroporation** Therapy (EPT) is currently being used in clinical trials for the treatment of a number...

...a substantially higher uptake of the chemotherapeutic drug by the cancer cells, thereby significantly enhancing **cell death** beyond conventional methods," said Dr. Gunter Hofmann, Genetronics Chairman and Chief Scientific Officer. "This patent...

...multi-site Phase II clinical trials in the U.S. and Canada using its proprietary **Electroporation** Therapy to treat patients with squamous cell carcinoma of the head and neck who have...

...Kaposi's sarcoma or melanoma.
In addition to oncology, Genetronics is developing applications for its **electroporation** technology in the primary areas of cardiology, gene therapy, dermatology and transdermal drug delivery. Worldwide...

...in San Diego and is recognized worldwide as the technology leader in the field of **electroporation** . It has been working since 1991 to devise ways to use **Electroporation** Therapy to improve the treatment of catastrophic illnesses, including cancer.

Visit Genetronics' Website at http...

...site: http://www.genetronics.com/
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CO: Genetronics Biomedical Ltd.
ST: California
IN: MTC
SU: **PDT**

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8994 03/17/98 11:00 EST http://www.prnewswire.com

27/3,K/2 (Item 1 from file: 442)

00107713

Long-term Follow-up and Histological Changes of Superficial Nonmelanoma Skin Cancers Treated With Topical <unprintable>-Aminolevulinic Acid Photodynamic Therapy (ARTICLE)

FINK-PUCHES, REGINA; SOYER, HANS PETER; HOFER, ANGELIKA; KERL, HELMUT; WOLF, PETER
Archives of Dermatology
July, 1998; Study: tzd821
LINE COUNT: 00495

... **up and Histological Changes of Superficial Nonmelanoma Skin Cancers Treated With Topical <unprintable>-Aminolevulinic Acid** Photodynamic Therapy

Objective: To investigate the immediate and long-term effects of **photodynamic therapy** with <unprintable>-aminolevulinic acid (ALA- **PDT**) on superficial basal cell carcinomas (BCC) and superficial squamous cell carcinomas (SCC). Design: Retrospective study...
... rates in the long-term follow-up, as well as histological changes associated with ALA- **PDT** , were studied. Results: The complete primary response rate for all wave bands of light was...

... rank test). Histopathologic studies revealed a significant increase of fibrosis in the dermis after ALA- **PDT** and appearance of a sharp border between fibrotic and nonfibrotic tissue. In 15 of 16...

... revealed poor long-term cure rates for superficial BCC and SCC treated with topical ALA- **PDT** and visible light. The histopathologic observations showing remarkable fibrosis in the dermis indicated that the effect of ALA- **PDT** reached deeper than the initial depth of invasiveness of the neoplastic tissue, suggesting in turn that the poor long-term results of ALA- **PDT** cannot be explained by insufficient penetration of the therapy effect. Arch Dermatol. 1998;134:821...

... BCC) and squamous cell carcinomas (SCC), has led to the search for new therapeutic modalities. **Photodynamic therapy** with topically applied <unprintable>-aminolevulinic acid (ALA- **PDT**) is a novel form of therapy for neoplasms of the skin and other organs. The principle of ALA- **PDT** is that topically applied ALA is metabolized by the tumor cells into **photosensitizing** concentrations of endogenous porphyrins, particularly protoporphyrin IX. Irradiation with visible light then leads to the selective destruction of tumor tissue.1,2/ Therapy with ALA- **PDT** is effective for superficial nonmelanoma skin tumors, and high primary clinical response rates with excellent cosmetic results have been reported.1,3-5/ Although ALA- **PDT** is used today experimentally in many centers around the world,6/ most clinical studies of ALA- **PDT** of skin tumors have involved only a small number of cases and a clinical follow...

RESULTS

FLUORESCENCE AFTER ALA **PHOTOSENSITIZATION**

For 66 BCC, the amount of surface fluorescence at the lesion site after ALA **photosensitization** was rated in 2 (3%) as weak; 33 (50%), moderate; 29 (44%), strong; and 2...

... response rate for BCC was 86% (82/95) (Table 1). The cosmetic results after ALA- **PDT** were excellent. There was a statistically significant correlation of clinical response of BCC with lesion...

... suggest that high fluorescence and phototoxic reaction are the most important factors for successful ALA- **PDT** in BCC.

There was no statistically significant difference (P>.05, x/2/ test) among the...

...clinical response of SCC with lesion diameter, fluorescence, light dose, and phototoxic reaction of ALA- **PDT** . There was also no site dependence of the clinical response of SCC. The complete clinical...

...confidence interval, 7%-9%) for SCC (P<.001, log-rank test).

HISTOLOGICAL CHANGES AFTER ALA- **PDT** IN BCC AND SCC

In 16 of 36 recurrent BCC, we compared histological sections from punch biopsy specimens before ALA- **PDT** with sections from excised lesions (n,=,4) or punch biopsy specimens (n,=,12) after therapy...

... significant homogeneous fibrosis in the dermis in all 16 cases after, but not before, ALA- **PDT** (Table 3). In all cases, there was a sharp border between fibrotic and nonfibrotic tissue in the dermis after ALA- **PDT** . In 15 of 16 lesions, the depth of fibrosis after therapy (mean depth, 1.04...

... rank test). Figure 2 shows the histological changes in a BCC 2 years after ALA- **PDT** . Similar results were found in 9 SCC (comparison of sections of 9 punch biopsy specimens before ALA- **PDT** vs those of 5 punch biopsy specimens and 4 surgically excised lesions after therapy), but the fibrotic changes after ALA- **PDT** were not as prominent as in BCC (Table 4). There were no correlations of tumor...primary response rate and long-term recurrence rate of superficial BCC and SCC after ALA- **PDT** with polychromatic wave bands of light. The complete primary response was 86% for superficial BCC...

... months (P<.001, log-rank test). Thus, our present long-term results for topical ALA- **PDT** with polychromatic light in the treatment of superficial skin cancers are poor, particularly for SCC...

... been previous reports1,5,21-23/ on response rates for skin cancers treated with ALA- **PDT** . In an early report on topical ALA- **PDT** with polychromatic light, Kennedy et al1/ noted a 90% complete remission of BCC at a...

...and 5 (83.3%) of 6 superficial SCC at 4 to 8 weeks after ALA- **PDT** . After a follow-up of 6 months, Wennberg et al22/ reported a 92% cure rate ...

... filtered xenon lamp as the light source. Lui et al,23/ who performed topical ALA- **PDT** with polychromatic visible light greater than 570 nm, achieved a clinical complete response in 7...

... al first suggested that there might be an unacceptably high tumor recurrence rate following ALA- **PDT** . However, higher long-term cure rates were reported in certain studies of ALA- **PDT** using laser light. For instance, Svanberg et al4/ obtained a 100% cure rate for superficial BCC and 90% for Bowen disease after ALA- **PDT** using laser light emitted at 630 nm and a follow-up of 6 to 14...

... reported a cure rate of 87% for superficial BCC and 83% for SCC by repetitive **PDT** after topical application of ALA and irradiation with a 630-nm light, from data obtained...

...the other hand, Cairnduff et al,24/ who also used 630-nm light for ALA- **PDT** , showed that only 50% of patients with superficial BCC remained disease-free at a median follow-up of 17 months. Thus, the better results achieved in the ALA- **PDT** studies by Svanberg and Calzavara-Pinton cannot be solely attributed to the use of laser...

... results demonstrate that long-term follow-up is necessary to evaluate the effect of ALA- **PDT** .

One factor that may have contributed to the failure of ALA- **PDT** is insufficient marking of tumors by protoporphyrin IX.25/ Indeed, Martin et al25/ previously demonstrated...

...topical ALA delivered with the present photodynamic protocols may not be a reliable regimen for **PDT** of BCC. Alternatively, they suggested that superficial tumors might contain tumor structures that lie too deep in the skin to be accessible to the topical ALA- **PDT** effect.

Our histopathologic studies indicated that ALA- **PDT** induces remarkable changes within the dermis of treated skin. In all 16 cases of BCC... the photodynamic threshold-dose, ie, the product of light and porphyrin accumulation that causes the **death** of **cells** and tissue.26/ In 15 of 16 BCC examined, the depth of fibrosis after ALA- **PDT** was greater than tumor thickness before therapy (Table 3). Similar results were found in SCC...

... fibrosis was not as marked as in BCC (Table 4). These observations indicated that ALA- **PDT** induced changes within the skin that reached deeper than the tumor cells of superficial BCC and SCC. Thus, the poor long-term results of ALA- **PDT** in the present study cannot be easily explained by insufficient penetration of the therapy effect.

The mechanism of ALA- **PDT** -induced fibrosis remains unclear at present. However, sclerotic skin changes with thickening of collagen bundles...

... theory suggests that transforming growth factor B is involved in the control of regression and **cell death** by apoptosis, which is a major determinant of growth in normal tissues and tumors.30/ We speculate that **PDT** by the application of ALA and irradiation by visible light might induce similar processes on...

...the tissue.

In conclusion, our study indicates that the long-term results of topical ALA- **PDT** with polychromatic light on superficial BCC and SCC are unsatisfactory at present. To improve ALA- **PDT** , other means of applying ALA, other vehicles for ALA, or both, supportive **iontophoresis** , and the use of chemical porphyrin inducers need to be studied. A recent study31/ indeed...

... that the application of desferrioxamine mesylate, an agent for forming iron complexes, may optimize ALA- **PDT** of skin cancers. Another suggestion for achieving better penetration is the use of curettage before **PDT** .22/ Ongoing studies, for instance, show that intralesional application of ALA in aqueous solution 4...

... the use of monochromatic laser light is superior to that of polychromatic light in ALA- **PDT** .

Accepted for publication March 6, 1998.

Corresponding author: Peter Wolf, MD, Department of Dermatology, University...

...Austria (e-mail: peter.wolf @kfunigraz.ac.at).

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Fink-Puches R, Wolf P, Kerl H. **Photodynamic therapy** of superficial basal cell carcinoma by instillation of aminolevulinic acid and irradiation with visible light...

... cases because it had previously been found5/ that they can reduce pain caused by ALA- **PDT** . The distance from the irradiation field to the lens ranged from 10 to 30 cm...570 nm (n,=,1), or greater than 610 nm (n,=,8) (Table 1).

During ALA- **PDT** , the fluorescence of the treated lesions was determined under a Wood light at regular 5...

...edema; and 4, vesiculation.

ASSESSMENT OF PRIMARY CLINICAL RESPONSE

Two to 4 weeks after ALA- **PDT** , clinical response to therapy was evaluated. Complete response was defined as the absence of a...

27/3,K/3 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals

00097776

Treatment of Kaposi's Sarcoma (ARTICLE)

Archives of Dermatology
Mar, 1996; Editorial Review: tzd327
LINE COUNT: 00521

... dye laser is effective for cutaneous macular lesions, but recurrences are noted within 3 months. **Photodynamic therapy** may also be used.

Intralesional cytotoxic chemotherapy (vinblastine is the most commonly used) is fast...

... Less favorable results were obtained witha combination of dimethyl sulfoxide, hydrocortisone acetate, and fraxiparin./21/ **Iontophoresis** is another experimental noninvasive method; successful vinblastine **iontophoresis** was noted in 31 patientswith AIDS-KS./22/

Radiotherapy is an important treatment, used for...setting.

Phosphorothioate antisense oligonucleotide directed against basic fibroblast growth factor was tested in AIDS-KS **cells** derived from several patients. It **inhibited** both **cell growth** and the angiogenic activity, and in addition it inhibited the induction of KS-like lesions...AIDS patients. Dermatology. 1993;187:78.

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Smith KJ, Konzelman JL, Lombardo FA, et al. **Iontophoresis** of vinblastine into normal skin and for treatment of Kaposi's sarcoma inhuman immunodeficiency virus...

27/3,K/5 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals

00050217

In Vitro Photodynamic Treatment of Normal and Human Papilloma Virus--Transfected Keratinocytes With Photofrin II and Red Light (Article)

Bernstein, Eric F., MD; Glass, Joseph M.; DeGraff, William G.; Schlegel, Richard, MD; Black, Christopher, PhD; Fisher, Joyce M.; Cook, Susan N.; Glatstein, Eli, MD; Russo, Angelo, PhD, MD; Mitchell, James B., PhD
Archives of Dermatology
1991; 127: 683 (5)

Photodynamic therapy involves the use of light of appropriate

wavelength to excite a **photosensitizer** to result in tissue destruction. The photosentisizer dihematoporphyrin ether and red light were used to...

... were sensitive to treatment, normal keratinocytes retained more dihematoporphyrin ether and were more sensitive to **photodynamic therapy** than were transfected cells. In vitro data fail to show the selective retention of dihematoporphyrin...

... despite previously published in vivo data to the contrary. Dihematoporphyrin ether retention and thus selective **photosensitivity** of papillomas in vivo is not caused by individual cellular differences in the processing of...

Photodynamic therapy (**PDT**) involves the use of light of appropriate wavelength to excite a photosentisizer to result in tissue destruction. \1,2 Once excited, the **photosensitizer** transfers the absorbed light energy to oxygen, producing a singlet oxygen species. Singlet oxygen then ...

The photosentisizer hematoporphyrin derivative (HPD) has been used in almost all clinical applications of **PDT** . A more purified form of HPD that is high in dihematoporphyrin ethers/esters (DHEs) is...

... 1,3/ Cutaneous malignant neoplasms, which are easily accessible to light, are particularly suited to **PDT** . Basal cell carcinoma, squamous cell carcinoma, melanoma, mycosis fungoides, Kaposi's sarcoma, metastatic breast carcinoma, and Bowen's disease have all been successfully treated with **PDT** . /3-8/ In addition, HPD has been shown to selectively localize in viral-induced papillomas...

... in rabbits /9,10/ and laryngeal papillomas in humans /11/ have been successfully treated with **PDT** . Trials are currently under way to study treatment of human genital papilloma virus infection with...

... all the cells in a given tissue. Isolated tumor or infected cells may lack selective **photosensitivity** if present before substantial architectural or vascular changes have occurred. We investigated DHE uptake and **PDT** -induced cytotoxic effects in normal human papilloma virus type 18 (HPV...

... exposed to increasing amounts of red light. Then, DHE uptake studies were performed simultaneously with **cell survival** studies on the same batch of cells and lots of DHE. Normal keratinocytes showed increased...

... 3 and 7. Keratinocytes transfected with either HPV-18 or HPV-16 were created by **electroporation** of normal keratinocytes with HPV DNA, as previously described. /15,16/ The resulting cell lines...

... incubated for 64 hours in the dark after light treatment and then were assayed for **survival** . **Survival** Assay **Cell survival** was assayed with 3-(4, 5-dimethylthizol-2-yl)-2, 5-diphenyltetrazolium bromide or MTT to blue, indirectly measuring **cell survival** . Fifty microliters of an MTT solution (2 mg/mL) was added to each cell-containing...

...with controls receiving neither light treatment nor DHE exposure. Normal keratinocytes were more sensitive to **PDT** than were HPV-18-transfected keratinocytes (Fig 1). Transfected keratinocytes required 1.4 times more...

... 02). This increased DHE uptake in normal keratinocytes is reflected in their greater susceptibility to **PDT** . Repeated studies yielded qualitatively similar results. Uptake After 24-Hour Efflux Period The HPV-16...

... modality for HPV infection due to the ability of DHE to selectively accumulate in tumors. **Photodynamic therapy** might allow for substantial sparing of normal tissue, an advantage over most currently used modalities. In addition, **PDT** produces no smoke or plume. Human papilloma varius DNA has been found in the vapor from carbon dioxide laser-treated verrucae /25/; **PDT** is free from this potential hazard. Shikowitz et al /9,10/ investigated the effect of **PDT** in rabbits infected with the cottontail

rabbit papilloma virus. Treated papillomas regressed, ...patients were clinically free of papillomas 13 months after treatment. We compared the effect of **PDT** combined with DHE on keratinocytes vs keratinocytes transfected with HPV. We chose HPV-18 and...

... of their role in human carcinogenesis. Although in vivo systems demonstrate and increased response to **PDT** in tumors and papillomas compared with normal tissues, in vitro data coparing tumor cells and...

... no difference in uptake or retention of HPD. Perry et al /28/ compared uptake and **photosensitivity** of lung cancer cell lines and normal fibroblasts and found fibroblasts to retain more DHE...

... RNA oncogenic virus. They found the transfected cells to be more sensitive to HPD-induced **PDT** , but they failed to take into account differences in cell volume or protein content, a...

... a comparison can be made. /12/. In our studies, normal keratinocytes were more susceptible to **PDT** than were their HPV-18-transfected counterparts. The increased sensitivity of normal keratinocytes is supported...

... and human papillomas. although Glassberg et al /13/ were able to show differential in vitro **photosensitivity** of fibrosarcoma cells compared with fibroblasts after an 8- or 24-hour efflux period in...

...of Glassberg et al may be due to the fact that we used a different **photosensitizer** and different cell lines. Tissue retention of DHE appears to be mediated by multiple factors...

... tissue. Gomer et al /30/ have shown vascular endothelial cells to be more sensitive to **PDT** than either smooth-muscle or fibroblast cell lines treated under identical conditions. They believed that this difference may play a role in the vascular damage seen after **PDT** . Our work suggests that the mechanism of selective uptake of HPD into papillomas in vivo...

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Set	Items	Description
S1	104750	CELL? ?
S2	110793	SURVIV?
S3	122725	DEATH OR DIE OR DIES OR DIED OR DYING
S4	458954	GROWTH
S5	47230	INHIBIT???
S6	188558	STOP? ? OR STOPP???
S7	6782	AVERT???
S8	126440	CHECK???
S9	16419	CURB???
S10	2704	APOPTOSIS
S11	912	S1(2N)S2
S12	3047	S1(3N)S3
S13	999	S1(2N)S4(3N)S5:S9
S14	4536	S11:S13
S15	391	ELECTROPORAT?
S16	313	(DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17	5	ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IONOTHERAPY OR ION()MEDICATION? ?
S18	183	IONTOPHORESIS
S19	847	S15:S18
S20	1112	PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21	1446	PHOTODYNAMIC()THERAPY OR PDT
S22	150	PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23	2483	S20:S22
S24	0	S14 AND S19 AND S23
S25	0	RD (unique items)

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Set     Items   Description
S1    1717149   CELL? ?
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S3     435011   DEATH OR DIE OR DIES OR DIED OR DYING
S4    1305423   GROWTH
S5     885542   INHIBIT???
S6      81476   STOP? ? OR STOPP???
S7       3479   AVERT???
S8      45458   CHECK???
S9      10195   CURB???
S10     73617   APOPTOSIS
S11     36490   S1(2N)S2
S12     46497   S1(3N)S3
S13     17328   S1(2N)S4(3N)S5:S9
S14     92879   S11:S13
S15      4806   ELECTROPORAT?
S16      1060   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17         2   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18      1482   IONTOPHORESIS
S19      7001   S15:S18
S20     10031   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21      3249   PHOTODYNAMIC()THERAPY OR PDT
S22      2066   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23     12960   S20:S22
S24         2   S14 AND S19 AND S23
S25         2   RD (unique items)
```

25/7/1 (Item 1 from file: 71) a duplicate of 25/7/1 (2nd page of non-pat. lit. results)
DIALOG(R)File 71:ELSEVIER BIOBASE

00888920 1997064387
Electric field-enhanced activation of hematoporphyrin derivative: Effects on a human tumour cell line
Ward T.; Mooney D.; Flynn G.; McHale A.P.
ADDRESS: A.P. McHale, Sch Applied Biological Chemical Sci, University of Ulster, Coleraine BT52 1SA, United Kingdom
EMAIL: ap.mchalegulst.ac.uk
Journal: Cancer Letters, 113/1-2 (145-151), 1997, Ireland
PUBLICATION DATE: 19970000
CODEN: CALED
ISSN: 0304-3835
PUBLISHER ITEM IDENTIFIER: S0304383596045922
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 19

In a recent report we described the effects of combined electroactivation and photoactivation of hematoporphyrin derivative (HPD) on human erythrocytes and established that activation-induced cell lysis was more pronounced when both modes of activation were sequentially applied to the system. Here we demonstrate that electric field-induced activation of HPD-treated HeLa **cells** results in **cell death** . This effect is shown to be dependant on both electric field strength and on HPD concentration. In addition, we demonstrate that exposure of HPD-treated cells to short and intense **electric pulses** prior to photoactivation, results in increased cell mortality. The results confirm our earlier suggestion that HPD may be activated in the presence of an applied electric field. The results further suggest that activation of **photosensitizers** using combined exposure to electric fields and light may play an important role in increasing the efficiency of **photodynamic therapy** (**PDT**) in the treatment of cancer.

25/7/2 (Item 1 from file: 19)
DIALOG(R)File 19:Chem.Industry Notes

1381804
On the horizon
Journal: Biotech Pat News 14 (5) p. 12 Date: 20000500
ISSN: 0898-2813 CODEN: BPANEP

Genetronics Inc. (San Diego, CA) has applied for a patent covering a method for inhibiting cell growth or enhancing cell death by electroporation of a photosensitive agent in a cell and photo-activation of the agent, useful for treating cancers and tumors. (US appl. 90751; WO Publication 200000250).

File 155:MEDLINE(R) 1966-2002/Dec W5

Set	Items	Description
S1	5826	'PHOTODYNAMIC THERAPY' OR 'PHOTOCHEMOTHERAPY'
S2	193270	R1:R7
S3	2940	R1:R2
S4	56019	R1:R3
S5	0	S1 AND S3 AND (S2 OR S4)
S6	1	S1 AND S3
S7	212	(S2 OR S4) AND S3
S8	118	S2 AND S3
S9	6932	PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY OR PHOTODYNAMIC()THERAPY OR PDT
S10	12387	PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S11	0	S7 AND S9:S10
S12	3205	ELECTROPORAT? OR ELECTRIC??()PATCH OR IONOTOPHORESIS OR IONOTHERAPY OR IONTOTHERAPY OR IONIC()MEDICATION? ?
S13	1233	(DC OR HIGH()VOLTAGE OR ELECTRIC??)()PULSE? ?
S14	4223	S3 OR S12 OR S13
S15	0	S2 AND S14 AND (S1 OR S9 OR S10)

6/3,K/1
DIALOG(R)File 155:MEDLINE(R)

11214168 21235670 PMID: 11337735
In situ ablation of hepatic tumors.
Cuschieri A
Department of Surgery and Molecular Oncology, Ninewells Hospital and Medical School, University of Dundee, Dundee, Scotland.
Seminars in laparoscopic surgery (United States) Mar 2001, 8 (1) p25-41, ISSN 1071-5517 Journal Code: 9432584
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Descriptors: Cryosurgery; *Laparoscopy; *Laser Surgery; *Liver Neoplasms --surgery--SU; * **Photochemotherapy** ; Cryosurgery--methods--MT; **Electroporation** ; Temperature

```
File 155:MEDLINE(R) 1966-2002/Dec W5
File   5:Biosis Previews(R) 1969-2003/Jan W1
         (c) 2003 BIOSIS
File  73:EMBASE 1974-2003/Jan W1
         (c) 2003 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Jan W1
         (c) 2003 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 144:Pascal 1973-2003/Jan W1
         (c) 2003 INIST/CNRS
File   6:NTIS 1964-2003/Jan W2
         (c) 2003 NTIS, Intl Cpyrght All Rights Res
File   2:INSPEC 1969-2003/Jan W1
         (c) 2003 Institution of Electrical Engineers
File   8:Ei Compendex(R) 1970-2003/Jan W1
         (c) 2003 Elsevier Eng.  Info. Inc.
File  99:Wilson Appl. Sci & Tech Abs 1983-2003/Dec
         (c) 2003 The HW Wilson Co.
File  65:Inside Conferences 1993-2003/Jan W2
         (c) 2003 BLDSC all rts. reserv.
File  94:JICST-EPlus 1985-2003/Nov W1
         (c)2003 Japan Science and Tech Corp(JST)
File  35:Dissertation Abs Online 1861-2003/Dec
         (c) 2003 ProQuest Info&Learning

Set     Items   Description
S1   11861401   CELL? ?
S2    1567836   SURVIV?
S3    1708605   DEATH OR DIE OR DIES OR DIED OR DYING
S4    4591339   GROWTH
S5    4601992   INHIBIT???
S6     297231   STOP? ? OR STOPP???
S7      10574   AVERT???
S8     336947   CHECK???
S9       7364   CURB???
S10    328038   APOPTOSIS
S11    153509   S1(2N)S2
S12    237070   S1(3N)S3
S13     87174   S1(2N)S4(3N)S5:S9
S14    446009   S11:S13
S15     20994   ELECTROPORAT?
S16     14063   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17        36   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18     17303   IONTOPHORESIS
S19     50834   S15:S18
S20    104901   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21     28810   PHOTODYNAMIC()THERAPY OR PDT
S22     14422   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    130855   S20:S22
S24         5   S14 AND S19 AND S23
S25         2   RD (unique items)
S26   3641846   LIGHT OR LASER
S27         6   (S10 OR S14) AND S19 AND S23
S28         1   S27 NOT S24
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28/7/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09724254 Genuine Article#: 439DZ Number of References: 151
Title: The lipid bilayer concept and its experimental realization: from soap bubbles, kitchen sink, to bilayer lipid membranes
Author(s): Tien HT (REPRINT) ; Ottova AL
Corporate Source: Michigan State Univ,Dept Physiol, Membrane Biophys Lab Giltner Hall,E Lansing//MI/48824 (REPRINT); Michigan State Univ,Dept Physiol, Membrane Biophys Lab Giltner Hall,E Lansing//MI/48824; Slovak Tech Univ,Dept Microelect, Ctr Interface Sci,Bratislava//Slovakia/
Journal: JOURNAL OF MEMBRANE SCIENCE, 2001, V189, N1 (JUL 31), P83-117
ISSN: 0376-7388 Publication date: 20010731
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: REVIEW
Abstract: The inspiration for lipid bilayer research, without question, comes from the biological world. Although self-assembled bilayer lipid membranes (BLMs) in vitro, were first reported in 1961, experimental scientists have been dealing with BLM-type interfacial adsorption phenomena since Robert Hooke's time (1672). BLMs (of planar lipid bilayers) have been used in a number of applications ranging from basic membrane biophysics including transport. practical AIDS research, and 'microchips' studies, to the conversion of solar energy via water photolysis, to biosensor development using supported bilayer lipid membranes (s-BLMs), and to photobiology comprising **apoptosis** and **photodynamic therapy** . This paper presents an overview of the origin of the lipid bilayer concept and its experimental realization, as well as the studies of our laboratory and recent research of others on the use of BLMs as models of certain biomembranes. In addition, we describe briefly our present work on supported BLMs as biosensors and molecular devices; the experiments carried out in close collaboration with colleagues on s-BLMs are delineated. (C) 2001 Elsevier Science B.V. All rights reserved.

```
File  95:TEME-Technology & Management 1989-2003/Dec W5
         (c) 2003 FIZ TECHNIK
File  98:General Sci Abs/Full-Text 1984-2003/Dec
         (c) 2003 The HW Wilson Co.
File   9:Business & Industry(R) Jul/1994-2003/Jan 13
         (c) 2003 Resp. DB Svcs.
File  16:Gale Group PROMT(R) 1990-2003/Jan 14
         (c) 2003 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2003/Jan 13
         (c)2003 The Gale Group
File 621:Gale Group New Prod.Annou.(R) 1985-2003/Jan 13
         (c) 2003 The Gale Group
File 636:Gale Group Newsletter DB(TM) 1987-2003/Jan 14
         (c) 2003 The Gale Group
File 149:TGG Health&Wellness DB(SM) 1976-2003/Dec W5
         (c) 2003 The Gale Group
File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Jan W2
         (c) 2003 ESPICOM Bus.Intell.
File  20:Dialog Global Reporter 1997-2003/Jan 14
         (c) 2003 The Dialog Corp.
File  15:ABI/Inform(R) 1971-2003/Jan 14
         (c) 2003 ProQuest Info&Learning
File  88:Gale Group Business A.R.T.S. 1976-2003/Jan 08
         (c) 2003 The Gale Group
File 442:AMA  Journals 1982-2003/Feb B2
         (c)2003 Amer Med Assn -FARS/DARS apply
File 444:New England Journal of Med. 1985-2003/Jan W2
         (c) 2003 Mass. Med. Soc.

Set     Items   Description
S1    1249034   CELL? ?
S2    1274552   SURVIV?
S3    2890450   DEATH OR DIE OR DIES OR DIED OR DYING
S4    5744595   GROWTH
S5     404427   INHIBIT???
S6    2339565   STOP? ? OR STOPP???
S7     100209   AVERT???
S8    1798780   CHECK???
S9     237201   CURB???
S10     23060   APOPTOSIS
S11      9002   S1(2N)S2
S12     32363   S1(3N)S3
S13      8322   S1(2N)S4(3N)S5:S9
S14     45360   S11:S13
S15      2748   ELECTROPORAT?
S16      3631   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17        23   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18      1150   IONTOPHORESIS
S19      7214   S15:S18
S20     11275   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21    156608   PHOTODYNAMIC()THERAPY OR PDT
S22      1175   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23    166985   S20:S22
S24        15   S14 AND S19 AND S23
S25        11   RD (unique items)
S26   2525664   LIGHT OR LASER
S27         2   ((S10 OR S14) AND S19 AND S23) NOT S24
S28         1   S26 AND S27
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28/3,K/1 (Item 1 from file: 636)
DIALOG(R)File 636:Gale Group Newsletter DB(TM)

03837983 Supplier Number: 48337603 (USE FORMAT 7 FOR FULLTEXT)
OTHER NEWS TO NOTE
BIOWORLD Today, v9, n42, pN/A
March 5, 1998
Language: English Record Type: Fulltext
Document Type: Magazine/Journal; Trade
Word Count: 800

(USE FORMAT 7 FOR FULLTEXT)
TEXT:
...of action, including modulation of the cellular levels of growth factors and their receptors, and **apoptosis** . * EntreMed Inc., of Rockville, Md., received orphan drug designation for thalidomide as a treatment for...

...and examine marketing and partnership opportunities in Europe. The clinical trials will utilize Genetronics' proprietary **electroporation** therapy in cancer patients. * Intercardia Inc., of Research Triangle Park, N.C., entered a definitive...

...brain tumor patients. The study will be conducted at the Royal Melbourne Hospital in Australia. **Photodynamic therapy** will be used, in which **light** -activated drugs and non-thermal **light** are deployed to attack cancer cells. * Siga Pharmaceuticals Inc., of New York, said it will...

```
File 369:New Scientist 1994-2003/Jan W1
         (c) 2003 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
File 135:NewsRx Weekly Reports 1995-2003/Jan W1
         (c) 2003 NewsRx
File 129:PHIND(Archival) 1980-2003/Jan W1
         (c) 2003 PJB Publications, Ltd.
File 187:F-D-C Reports 1987-2003/Dec W4
         (c) 2003 F-D-C Reports Inc.
File 429:Adis Newsletters(Archive) 1982-2003/Jan 14
         (c) 2003 Adis Intl. Ltd.
File 624:McGraw-Hill Publications 1985-2003/Jan 14
         (c) 2003 McGraw-Hill Co. Inc
File 635:Business Dateline(R) 1985-2003/Jan 14
         (c) 2003 ProQuest Info&Learning

Set     Items   Description
S1     104755   CELL? ?
S2     110803   SURVIV?
S3     122731   DEATH OR DIE OR DIES OR DIED OR DYING
S4     458999   GROWTH
S5      47230   INHIBIT???
S6     188573   STOP? ? OR STOPP???
S7       6783   AVERT???
S8     126462   CHECK???
S9      16419   CURB???
S10      2704   APOPTOSIS
S11       912   S1(2N)S2
S12      3047   S1(3N)S3
S13       999   S1(2N)S4(3N)S5:S9
S14      4536   S11:S13
S15       391   ELECTROPORAT?
S16       313   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17         5   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18       183   IONTOPHORESIS
S19       847   S15:S18
S20      1112   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21      1446   PHOTODYNAMIC()THERAPY OR PDT
S22       150   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23      2483   S20:S22
S24         0   S14 AND S19 AND S23
S25         0   RD (unique items)
S26    202092   LIGHT OR LASER
S27         0   (S10 OR S14) AND S19 AND S23 AND S26
```

```
File  50:CAB Abstracts 1972-2003/Dec
         (c) 2003 CAB International
File  71:ELSEVIER BIOBASE 1994-2003/Jan W2
         (c) 2003  Elsevier Science B.V.
File 143:Biol. & Agric. Index 1983-2003/Dec
         (c) 2003 The HW Wilson Co
File 162:CAB Health 1983-2002/Nov
         (c) 2002 CAB International
File 156:ToxFile 1965-2002/Nov W3
         (c) format only 2002 The Dialog Corporation
File 172:EMBASE Alert 2003/Jan W2
         (c) 2003 Elsevier Science B.V.
File  19:Chem.Industry Notes 1974-2003/ISS 200302
         (c) 2003 Amer.Chem.Soc.
File  91:MANTIS(TM) 1880-2002/Oct
         2002 (c) Action Potential
File 164:Allied & Complementary Medicine 1984-2002/Dec
          (c) 2002 BLHCIS
File 467:ExtraMED(tm) 2000/Dec
         (c) 2001 Informania Ltd.
File  42:Pharmaceuticl News Idx 1974-2003/Jan W1
         (c)2003 ProQuest Info&Learning
File 285:BioBusiness(R) 1985-1998/Aug W1
         (c) 1998 BIOSIS
File 358:Current BioTech Abs 1983-2002/Dec
          (c) 2002 DECHEMA
File 583:Gale Group Globalbase(TM) 1986-2002/Dec 13
         (c) 2002 The Gale Group
File 315:ChemEng & Biotec Abs 1970-2002/Dec
         (c) 2002 DECHEMA

Set     Items   Description
S1    1717149   CELL? ?
S2     324724   SURVIV?
S3     435011   DEATH OR DIE OR DIES OR DIED OR DYING
S4    1305423   GROWTH
S5     885542   INHIBIT???
S6      81476   STOP? ? OR STOPP???
S7       3479   AVERT???
S8      45458   CHECK???
S9      10195   CURB???
S10     73617   APOPTOSIS
S11     36490   S1(2N)S2
S12     46497   S1(3N)S3
S13     17328   S1(2N)S4(3N)S5:S9
S14     92879   S11:S13
S15      4806   ELECTROPORAT?
S16      1060   (DC OR HIGH()VOLTAGE OR ELECTRIC??)()(PULSE OR PULSES)
S17         2   ELECTRIC??()PATCH?? OR IONOTPHORESIS OR IONTOTHERAPY OR IO-
              NOTHERAPY OR ION()MEDICATION? ?
S18      1482   IONTOPHORESIS
S19      7001   S15:S18
S20     10031   PHOTOSENSITI? OR SENSITI?ER? ?(5N)PHOTOOXID?
S21      3249   PHOTODYNAMIC()THERAPY OR PDT
S22      2066   PHOTOPHORESIS OR PHOTORADIOTHERAPY OR PHOTOCHEMOTHERAPY
S23     12960   S20:S22
S24         2   S14 AND S19 AND S23
S25         2   RD (unique items)
S26    341049   LASER OR LIGHT
S27         1   (S10 OR S14) AND S19 AND S23 AND S26
S28         0   S27 NOT S24
```

27/3,K/1 (Item 1 from file: 71) a duplicate
DIALOG(R)File 71:ELSEVIER BIOBASE

00888920 1997064387

Electric field-enhanced activation of hematoporphyrin derivative: Effects on a human tumour cell line

Ward T.; Mooney D.; Flynn G.; McHale A.P.
ADDRESS: A.P. McHale, Sch Applied Biological Chemical Sci, University of Ulster, Coleraine BT52 1SA, United Kingdom
EMAIL: ap.mchalegulst.ac.uk

Journal: Cancer Letters, 113/1-2 (145-151), 1997, Ireland
PUBLICATION DATE: 19970000
CODEN: CALED
ISSN: 0304-3835
PUBLISHER ITEM IDENTIFIER: S0304383596045922
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 19

...to the system. Here we demonstrate that electric field-induced activation of HPD-treated HeLa **cells** results in **cell death** . This effect is shown to be dependant on both electric field strength and on HPD concentration. In addition, we demonstrate that exposure of HPD-treated cells to short and intense **electric pulses** prior to photoactivation, results in increased cell mortality. The results confirm our earlier suggestion that...

...in the presence of an applied electric field. The results further suggest that activation of **photosensitizers** using combined exposure to electric fields and **light** may play an important role in increasing the efficiency of **photodynamic therapy** (**PDT**) in the treatment of cancer.

DESCRIPTORS:
Hematoporphyrin derivative; Electric; Fields; Cancer; **Photodynamic** ; **Therapy** ; HeLa

File 350:Derwent WPIX 1963-2002/UD,UM &UP=200303
(c) 2003 Thomson Derwent
File 347:JAPIO Oct 1976-2002/Sep(Updated 030102)
(c) 2003 JPO & JAPIO
File 371:French Patents 1961-2002/BOPI 200209
(c) 2002 INPI. All rts. reserv.

Set	Items	Description
S1	123	AU='BERG H':AU='BERG H V D'
S2	1	AU='LAMBREVA M'
S3	1	S1 AND S2

3/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012988790
WPI Acc No: 2000-160643/200014
Inhibiting cell growth or enhancing cell death by electroporation of a photosensitive agent in a cell and photo-activation of the agent, useful for treating cancers and tumors
Patent Assignee: GENETRONICS INC (GENE-N)
Inventor: **BERG H ; LAMBREVA M**
Number of Countries: 022 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200000250	A1	20000106	WO 99US14202	A	19990625	200014	B
AU 9950841	A	20000117	AU 9950841	A	19990625	200026	
EP 1100576	A1	20010523	EP 99935345	A	19990625	200130	
			WO 99US14202	A	19990625		

Priority Applications (No Type Date): US 9890751 P 19980626
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200000250	A1	E	41	A61N-001/00	
Designated States (National): AU CA JP					
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
AU 9950841	A			A61N-001/00	Based on patent WO 200000250
EP 1100576	A1	E		A61N-001/00	Based on patent WO 200000250
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

Abstract (Basic): WO 200000250 A1

NOVELTY - Inhibition of cell growth or enhancement of cell death comprises providing a photosensitive agent to a cell and applying an electric pulse of a sufficient strength and duration to the cell to electroporate it with the photosensitive agent. Light of activatable wavelength is applied to the cell, thus activating the agent and inhibiting cell growth or enhancing cell death.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an apparatus for treating a cell proliferative disorder in a subject, comprising (a) an electrode capable of applying an electric pulse of sufficient strength and duration to electroporate a cell in the subject; and (b) a light conductor for applying light of an activating wavelength to the electroporated cell.

USE - The invention is used for inhibiting cell growth or enhancing cell death. It may also be used for treating a cell proliferative disorder which may be benign or a cancer including skin cancer, a solid tumor, a metastasizing cancer, or hematopoietic cancer specifically histiocytic lymphoma.

ADVANTAGE - Electroporation of a photosensitive agent in a cell and subsequent activation of the agent provides more effective killing of the electroporated cell than cells exposed to a photosensitive agent alone. The invention employs lower doses of a photosensitive agent than is typically used in photooxidizing treatment therapies. The addition of heat promotes or accelerates diffusion of the photosensitive agent, thus providing an additive or synergistic effect. The invented method affords exquisite control of inhibiting cell growth or enhancing cell death of undesirable or hyperproliferative cells while avoiding surrounding healthy cells or tissue, since the invention employs electroporation and photosensitive agents that are nontoxic in the unactivated state.

pp; 41 DwgNo 0/3
Derwent Class: B05; P34; S05
International Patent Class (Main): A61N-001/00

File 348:EUROPEAN PATENTS 1978-2002/Dec W03
(c) 2002 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030109,UT=20030102
(c) 2003 WIPO/Univentio

Set	Items	Description
S1	6	AU='BERG HERMANN':AU='BERG HERMANN OTTO DIPL ING'
S2	2	AU='LAMBREVA MAYA'
S3	2	S1 AND S2
S4	4	S1:S2 NOT S3 - not relevant

3/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2002 European Patent Office. All rts. reserv. a duplicate

01125157
SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT
ZYTOTOXISCHE SYNERGIE VON PHOTODYNAMISCHEN UND ELEKTROPERMEATIONSEFFEKTEN AUF DIE ZELLVITALITAT
SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE
PATENT ASSIGNEE:
Genetronics, Inc., (2013211), 11199-A Sorrento Valley Road, San Diego, CA 92121-1334, (US), (Applicant designated States: all)
INVENTOR:
LAMBREVA, Maya , Dianabad, BL. 39-40, Vh. 12, AP. 194, 1172 Sofia, (BG)
BERG, Hermann , Greifenberg Strasse 15, D-07749 Jena, (DE
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1100576 A1 010523 (Basic)
WO 200000250 000106
APPLICATION (CC, No, Date): EP 99935345 990625; WO 99US14202 990625
PRIORITY (CC, No, Date): US 90751 P 980626
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61N-001/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

3/3,AB/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2003 WIPO/Univentio. All rts. reserv. a duplicate

00536877
SYNERGISM OF PHOTODYNAMIC AND ELECTROPERMEATION EFFECTS ON CELL VITALITY AS A NOVEL CYTOTOXIC AGENT
SYNERGIE CYTOTOXIQUE DE LA PHOTODYNAMIQUE ET DE L'ELECTROPERMEATION SUR LA VITALITE CELLULAIRE
Patent Applicant/Assignee:
GENETRONICS INC,
Inventor(s):
LAMBREVA Maya ,
BERG Hermann
Patent and Priority Information (Country, Number, Date):
Patent: WO 200000250 A1 20000106 (WO 0000250)
Application: WO 99US14202 19990625 (PCT/WO US9914202)
Priority Application: US 9890751 19980626
Designated States: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 9253

English Abstract
The present invention is based on the discovery that electroporation of a photosensitive agent in a cell and subsequent activation of the agent provides more effective killing of the electroporated cell than cells exposed to a photosensitive agent alone. The invention provides a method and apparatus for inhibiting cell growth or enhancing cell death. The method includes providing a photosensitive agent to a cell; applying an electric pulse to the cell of a sufficient strength and duration to electroporate the cell with the photosensitive agent; and applying light of an activatable wavelength to the cell thereby activating the agent and inhibiting cell growth or enhancing cell death.

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File 155:MEDLINE(R) 1966-2002/Dec W5
File   5:Biosis Previews(R) 1969-2003/Jan W1
         (c) 2003 BIOSIS
File  73:EMBASE 1974-2003/Jan W1
         (c) 2003 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Jan W1
         (c) 2003 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info

Set     Items   Description
S1        521   AU='BERG H'
S2         33   AU='BERG HERMANN'
S3        104   AU='BERG H.'
S4          8   AU='LAMBREVA M':AU='LAMBREVA MD'
S5          2   S1:S3 AND S4
S6          1   RD (unique items)
S7      17288   ELECTROPORAT?
S8         48   S1:S4 AND S7
S9    9611350   CELL OR CELLS
S10        43   S8 AND S9
S11        12   S10/2003 OR S10/2002 OR S10/2001 OR S10/2000 OR S10/1999
S12        31   S10 NOT S11
S13        15   RD (unique items)
```

12261429 BIOSIS NO.: 200000014931

Increased incorporation of photosensitive dyes into yeast cells by electroporation.

AUTHOR: **Lambreva Maya** ; Zhou Aihua; Hoenes Ingeburg; **Berg Hermann** (a
AUTHOR ADDRESS: (a)Laboratory of Bioelectrochemistry, Jena**Germany

JOURNAL: Electro- and Magnetobiology 18 (3):p269-275 Nov., 1999
ISSN: 1061-9526
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Photooxidation by natural and synthetic sensitizers as a method of cell destruction also shows practical possibilities, whereas electroporation accelerates drug incorporation. Both agents were combined for the synergistic destruction of yeast cells. The sensitizers thiopyronin, protoporphyrin, and actinomycin D, a cancerostatic peptide dye, act according to type 1 or type 2 photochemical mechanisms. Two series of applications of single DC pulses and continuous visible light were performed with the result that this synergism yielded an efficacy up to ten times higher than the ordinary irradiation of intact yeast cells. This combination of electricity and light can be the starting point for an improved photodynamic therapy.

13/6/1 (Item 1 from file: 155)
09759066 98186865 PMID: 9518518
Interleukin-10 expression is induced by increase of intracellular calcium levels in the monocytic cell **line U937.**
May 1998

13/6/2 (Item 2 from file: 155)
08684825 96053929 PMID: 7550757
Electrofusion of yeast protoplasts.
1995

13/6/3 (Item 1 from file: 5)
11844847 BIOSIS NO.: 199900090956
Uptake of sensitizer by electroporated **yeast** cells .
1998

13/6/4 (Item 2 from file: 5)
11844836 BIOSIS NO.: 199900090945
Electropermeabilization and electrofusion of human cells **modified by anaesthetic agents.**
1998

13/6/5 (Item 3 from file: 5)
11844832 BIOSIS NO.: 199900090941
Electroporation **induced gene expression: A case study on interleukin-10: The Luigi Galvani prize lecture 1998.**
1998

13/6/6 (Item 4 from file: 5)
11799241 BIOSIS NO.: 199900045350
Electropermeabilization and electrofusion of human lymphoma cells **modified by proteolytic enzymes.**
1998

13/6/7 (Item 5 from file: 5)
11441431 BIOSIS NO.: 199800222763
Electrofusion of protoplasts modified by protein adsorption.
1998

13/6/8 (Item 6 from file: 5)
11440967 BIOSIS NO.: 199800222299
Electroporation **and fusion modified by nucleic acids and complexes.**
1998

13/6/9 (Item 7 from file: 5)
10753265 BIOSIS NO.: 199799374410
Electroporation **stimulates interleukin 10 production in human monocytic** cell **lines THP-1 and U937.**
1996

13/6/10 (Item 8 from file: 5)
10753082 BIOSIS NO.: 199799374227
Modification of electrofusion by proteins.
1996

13/6/11 (Item 9 from file: 5)

09993443 BIOSIS NO.: 199598448361
Possibilities and problems of low frequency weak electromagnetic fields in cell biology.
1995

13/6/12 (Item 1 from file: 73)
06722330 EMBASE No: 1997003789
Electroporation **stimulates interleukin 10 production in human** cell **lines THP-1 and U937**
1996

13/6/13 (Item 1 from file: 34)
07300981 Genuine Article#: 147XU Number of References: 13
Title: The influence of extracellular alkali and alkaline-earth ions on electropermeation of Saccharomyces cerevisiae (ABSTRACT AVAILABLE)
Publication date: 19981000

13/6/14 (Item 2 from file: 34)
02431191 Genuine Article#: LB186 Number of References: 12
Title: EFFECT OF ELECTRICAL ENERGY ON THE ELECTROPERMEABILIZATION OF YEAST-CELLS (Abstract Available)

13/6/15 (Item 3 from file: 34)
01202643 Genuine Article#: GE128 Number of References: 30
Title: MODIFICATION OF ELECTROFUSION OF BARLEY PROTOPLAST BY MEMBRANE-ACTIVE AGENTS (Abstract Available)
?t13/3,k/3,9,11,14

13/3,K/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11844847 BIOSIS NO.: 199900090956
Uptake of sensitizer by electroporated **yeast** cells .
AUTHOR: Wang Xing(a); Hones I; **Berg Hermann** (a
AUTHOR ADDRESS: (a)Biophys. Program, Dep. Physics, Nankai Univ., Tianjin 300071**China
JOURNAL: Bioelectrochemistry and Bioenergetics 47 (1):p175-177 Nov., 1998
ISSN: 0302-4598
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

Uptake of sensitizer by electroporated **yeast** cells .
...AUTHOR: **Berg Hermann**

ABSTRACT: The photodynamic effect on yeast (Saccharomyces cerevisiae) **cell** viability has been enhanced by **electroporation** treatment. Exponentially decaying high-voltage pulses caused temporary permeability changes on the **cell** walls, by which the uptake of the sensitizer thiopyronine (TP) has been accelerated. The total...

...effect after 5 min irradiation increased to more than 10 times, e.g., 75-80% **cells** are dead, as much as the control sample, which was treated only by TP and irradiation but without **electroporation** .
MAJOR CONCEPTS: Membranes (**Cell** Biology...
METHODS & EQUIPMENT: **electroporation** --...

...BTX Electro **Cell** Manipulator 600
MISCELLANEOUS TERMS: **cell** viability...

13/3,K/9 (Item 7 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

10753265 BIOSIS NO.: 199799374410
Electroporation **stimulates interleukin 10 production in human monocytic cell lines THP-1 and U937.**
AUTHOR: Lehmann Michael H(a); Hoeffken Klaus(a); **Berg Hermann**
AUTHOR ADDRESS: (a)Clinic Intern. Med. II, Friedrich Schiller Univ., Jena** Germany
JOURNAL: Bioelectrochemistry and Bioenergetics 41 (2):p227-229 1996
ISSN: 0302-4598
RECORD TYPE: Citation
LANGUAGE: English

Electroporation **stimulates interleukin 10 production in human monocytic cell lines THP-1 and U937.**
...AUTHOR: **Berg Hermann**
DESCRIPTORS:
...ORGANISMS: **cell** line...

... **cell** line
MISCELLANEOUS TERMS: ... **ELECTROPORATION** ;

13/3,K/11 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

09993443 BIOSIS NO.: 199598448361
Possibilities and problems of low frequency weak electromagnetic fields in cell biology.
AUTHOR: **Berg Hermann**
AUTHOR ADDRESS: Inst. Molecular Biotechnol., Lab. Bioelectrochemistry, 07745 Jena**Germany
JOURNAL: Bioelectrochemistry and Bioenergetics 38 (1):p153-159 1995
ISSN: 0302-4598
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

Possibilities and problems of low frequency weak electromagnetic fields in cell biology.
AUTHOR: **Berg Hermann**

ABSTRACT: In addition to its well-known applications in **electroporation** of **cell** membranes, the use of electrostimulation of cellular metabolisms by weak electromagnetic or electric fields as...

...possibility to electrostimulate reactions - e.g. the phosphorylation of the myosin light chain - in a **cell** -free system. In this system there is no membrane receiver for electromagnetic energy transformation and...
MAJOR CONCEPTS: **Cell** Biology...

...Membranes (**Cell** Biology...
MISCELLANEOUS TERMS: ... **CELL** -FREE SYNTHESIS

13/3,K/14 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

02431191 Genuine Article#: LB186 No. References: 12
Title: EFFECT OF ELECTRICAL ENERGY ON THE ELECTROPERMEABILIZATION OF YEAST-CELLS
Author(s): MURAJI M; TATEBE W; KONISHI T; FUJII T; **BERG H**
Corporate Source: OSAKA CITY UNIV,FAC ENGN,DEPT ELECT ENGN,SUMIYOSHI KU/OSAKA 558//JAPAN/; INST MOLEC BIOTECHNOL,BIOELECTROCHEM

LAB/JENA//GERMANY/
Journal: BIOELECTROCHEMISTRY AND BIOENERGETICS, 1993, V31, N1 (MAY), P77-84
ISSN: 0302-4598
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

Title: EFFECT OF ELECTRICAL ENERGY ON THE ELECTROPERMEABILIZATION OF YEAST-CELLS

Author(s): MURAJI M; TATEBE W; KONISHI T; FUJII T; **BERG H**

Abstract: A suspension of yeast **cells** (Saccharomyces cerevisiae) in NaCl solution was exposed to high voltage pulses under defined conditions. The results on perforation through the membrane and the **cell** wall structure (electropermeabilization) and the resealing process was presented. Capacitor discharges were applied to yeast **cells** in their logarithmic growth phase. A dye was added at a predetermined time after the electric pulse. Dyed and total (dyed plus undyed) yeast **cells** were counted microscopically and the rate was calculated. Dyed **cells** were assumed to have pores.

For simplicity, the time constant of the electric circuit was...

...the electrical energy is closely concerned with the electropermeabilization and resealing of the membrane and **cell** wall.

...Identifiers--HUMAN-ERYTHROCYTES; **ELECTROPORATION**; BREAKDOWN; HEMOLYSIS; FIELD